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For *in-vitro* diagnostic use

**Intended Use:**

23andMe® Carrier Status Tests for autosomal recessive conditions are qualitative *in vitro* molecular detection systems used for genotyping of clinically relevant variants in genomic DNA isolated from human saliva collected with the Oragene®-Dx model OGD-500.001. The tests are intended for adults, and not intended for copy number variation, cytogenetic, or biochemical testing.

**Summary and explanation of the test:**

23andMe Carrier Status Tests are tests you can order and use at home to learn about your DNA from a saliva sample collected using an FDA cleared collection device Oragene-Dx model OGD-500.001. The tests work by detecting specific gene variants. Your genetic results are returned to you in a secure online account on the 23andMe website.

**Indications for Use:**

See test-specific information for each test.

**Important:**

- Please follow the instructions in the DNA Collection Kit to ensure your DNA results can be processed and connected to your online account.
- Some people feel a little anxious about getting genetic health results. This is normal. If you feel very anxious, you should speak to your doctor or a genetic counselor prior to collecting your sample for testing. You may also consider getting your test done by your doctor.
- Your ethnicity may affect whether certain tests are relevant for you. Your ethnicity also may affect how your genetic health results are interpreted.
- These tests are intended only for autosomal recessive carrier screening in adults.
• If you have a family history of a condition, or think you have symptoms of a condition, consult with your healthcare provider about appropriate testing.
• The absence of a variant tested does not rule out the presence of other variants that may be disease-related.
• These tests are not intended to diagnose a disease or tell you anything about the health of your fetus.
• These tests will not tell you or your newborn child the risk of developing a particular disease later in life.
• These tests are not a substitute for visits to a health care professional. It is recommended that you consult with a health care professional if you have any questions or concerns about your results.
• These tests do not diagnose any health conditions. Results should be used along with other clinical information for any medical purposes.

Limitations:

• These tests do not detect all genetic variants related to these diseases.
• The American College of Medical Genetics (ACMG) and American Congress of Obstetricians and Gynecologists (ACOG) have issued recommendations for carrier testing of certain health conditions. Some of our tests may not cover all of the variants recommended for testing.
• These tests do not identify if a person has two copies of any variants.
• These tests may not be able to determine a result for all variants analyzed.
• The laboratory may not be able to process your sample. The probability that the laboratory cannot process your saliva sample can be up to 3%. If this happens, we will notify you by email and you may request one free replacement kit to provide us with a new sample.

Test performance

The performance of these tests was assessed only for the detection of the specific gene variants analyzed by each test in adults. Samples were collected using the Oragene-Dx saliva collection device (OGD-500.001). The samples were tested on the Illumina® Infinium BeadChip. Results were analyzed using the Illumina iScan System and GenomeStudio and Coregen software.

Clinical performance

The clinical performance and variants included for each test are supported by peer-reviewed scientific literature.

See test-specific information for each test.
Analytical performance

Accuracy
Accuracy studies were performed at two lab sites using samples with known variant status. Results of each 23andMe test were compared with sequencing results. Only samples that passed quality control and produced a genotype for both sequencing and the 23andMe test were included in the calculation for percent agreement. 23andMe test results demonstrated at least 99% agreement with sequencing.

Precision/Reproducibility
Precision studies were performed to understand the consistency of sample measurements when tested under different conditions. Human samples of known variant status were tested for precision. Testing was performed at two lab sites over five non-consecutive days with multiple operators. The testing used three lots of reagents and two sets of instruments at each lab site.

A total of 135 replicates were run for each sample tested. Any samples failing quality control acceptance criteria were retested per lab procedures. Only sample replicates that passed quality control and produced a genotype for the 23andMe test were included in the calculation for percent agreement. All test results demonstrated at least 99% agreement between replicates.

Limit of detection
A limit of detection study was performed to understand the lowest concentration of DNA needed for at least 95% concordant test results. The study was performed using six human cell line samples and three lots of reagents at each of two lab sites. The study yielded concordant test results for samples with a DNA concentration of 15 ng/µL.

Interferences
Studies were performed to determine whether substances that may be present in saliva affect results of the PGS Carrier Status tests. Four proteins that may be found in human saliva were added to saliva samples. These proteins did not affect test performance.

Studies were also performed to determine whether foreign substances found in saliva affect results of the PGS Carrier Status tests. Saliva samples were collected from five people at three time points. First, a sample was collected before consuming a substance. Then, a sample was collected immediately after consumption. Finally, a sample was collected thirty minutes after consumption.

The following conditions were tested:
• Eating food containing beef
• Eating food other than beef
• Drinking
• Chewing gum
• Using mouthwash
• Smoking
The studies indicated that saliva samples should be collected at least thirty (30) minutes after eating, drinking, chewing gum, using mouthwash, or smoking.

Another study was performed to assess the effects of five microbes that may be found in human saliva. The microbial DNA had no effect on the accuracy of the PGS Carrier Status tests.

**User studies**

*Saliva collection kit user study*

User studies were performed to assess how well people understand the saliva collection kit instructions and to assess the ability of lay users to provide samples adequate for testing. Study participants represented a wide range of demographic characteristics. Participants were asked to collect and mail a saliva sample and answer an online survey about the collection kit instructions from home. Saliva samples were processed according to standard laboratory procedures.

The overall comprehension rate on the collection kit instructions was 92.1% and greater than 97% of samples met all laboratory quality criteria, demonstrating that users from diverse backgrounds can understand the collection kit instructions and provide adequate saliva samples.

*PGS test report user comprehension study*

User comprehension studies were performed to assess how well people understand the PGS Carrier Status test reports. A diverse group of people answered questions about test reports in a controlled lab-based setting. Comprehension was tested through a two-step process. First, participants' understanding of genetics was tested prior to viewing the educational module and test reports. Second, participants were shown the educational module and the test reports. Participants then completed the test report comprehension survey.

The Bloom Syndrome test report and Cystic Fibrosis test report were included in these studies. Overall comprehension rates per test report concept averaged 92% across all concepts in both studies. Comprehension of three out of five concepts tested was significantly improved following participants seeing the education module.

**Specific test information**

-Agenesis of the Corpus Callosum with Peripheral Neuropathy
-ARSACS
-Autosomal Recessive Polycystic Kidney Disease
-Beta Thalassemia and Related Hemoglobinopathies
-Bloom Syndrome
-Congenital Disorder of Glycosylation Type 1a (PMM2-CDG)
-Cystic Fibrosis
-D-Bifunctional Protein Deficiency
-Dihydrolipoamide Dehydrogenase Deficiency
Familial Dysautonomia
Fanconi Anemia Group C
Glycogen Storage Disease Type Ia
Glycogen Storage Disease Type Ib
GRACILE Syndrome
Hereditary Fructose Intolerance
Leigh Syndrome, French Canadian Type
Limb-Girdle Muscular Dystrophy Type 2D
Limb-Girdle Muscular Dystrophy Type 2E
Limb-Girdle Muscular Dystrophy Type 2I
Maple Syrup Urine Disease Type 1B
MCAD Deficiency
Neuronal Ceroid Lipofuscinosis (CLN5-Related)
Neuronal Ceroid Lipofuscinosis (PPT1-Related)
Niemann-Pick Disease Type A
Nijmegen Breakage Syndrome
Nonsyndromic Hearing Loss and Deafness, DFNB1 (GJB2-Related)
Pendred Syndrome and DFNB4 Hearing Loss
Primary Hyperoxaluria Type 2
Rhizomelic Chondrodysplasia Punctata Type 1
Sickle Cell Anemia
Sjögren-Larsson Syndrome
Tay-Sachs Disease
Tyrosinemia Type I
Usher Syndrome Type 1F
Usher Syndrome Type 3A
Zellweger Syndrome Spectrum (PEX1-Related)

Agenesis of the Corpus Callosum with Peripheral Neuropathy (ACCPN)

Indications for Use

The 23andMe PGS Carrier Status Test for Agenesis of the Corpus Callosum with Peripheral Neuropathy (ACCPN) is indicated for the detection of the T813fsX813 variant in the SLC12A6 gene. This test is intended to be used to determine carrier status for ACCPN in adults, but cannot determine if a person has two copies of a tested variant. The test is most relevant for people of French Canadian descent.

Special considerations

- There are currently no professional guidelines in the U.S. for carrier testing for this condition.
**Clinical performance**

The variant covered by this test is mainly found in people of French Canadian descent. About 1 in 23 people (4.3%) with this ancestry from the Charlevoix/Saguenay-Lac-St.-Jean region of Quebec carries this variant.

**Frequency of SLC12A6 variants in 23andMe customers**

<table>
<thead>
<tr>
<th>Variant name</th>
<th>European</th>
<th>African American</th>
<th>Ashkenazi</th>
<th>East Asian</th>
<th>Hispanic or Latino</th>
<th>South Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>T813fsX813</td>
<td>0.01%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
</tr>
</tbody>
</table>

This test is expected to detect more than 99% of carriers of French Canadian descent for this condition.

**Pre-test and post-test carrier risks for the 23andMe PGS Carrier Status Test for ACCPN**

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Carrier detection rate for this test</th>
<th>Pre-test (average) carrier risk</th>
<th>Post-test carrier risk for result “0 Variants Detected”</th>
</tr>
</thead>
<tbody>
<tr>
<td>French Canadian</td>
<td>&gt;99%</td>
<td>1 in 23</td>
<td>1 in 22,000,000</td>
</tr>
<tr>
<td>Other ethnicities*</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

*This condition is not well studied in other ethnicities.

**Accuracy**

23andMe performed a method comparison study to assess the accuracy of the assay. Results of the test were compared with sequencing results for 47 samples with known variant status. Agreement between the two methods was >99% for all samples analyzed. The 95% confidence interval was 91.0% to 100%.

**Precision/Reproducibility**

A study was performed to assess the precision of the test. A total of 1,350 sample replicates were run across different testing conditions. This study yielded correct results for >99% of samples across all conditions tested. The study had >99% reproducibility and >99% repeatability.

**Selected References**


Additional references included in the test report.

ARSACS

*Indications for Use*

The 23andMe PGS Carrier Status Test for Autosomal Recessive Spastic Ataxia of Charlevoix-Saguenay (ARSACS) is indicated for the detection of the 6594delT variant in the SACS gene. This test is intended to be used to determine carrier status for ARSACS in adults, but cannot determine if a person has two copies of a tested variant. The test is most relevant for people of French Canadian descent.

*Special considerations*

- There are currently no professional guidelines in the U.S. for carrier testing for this condition.

*Clinical performance*

The 6594delT variant covered by this test is mainly found in people of French Canadian descent. About 1 in 22 people (4.55%) with this ancestry from the Charlevoix/Saguenay-Lac-St.-Jean region of Quebec carries this variant.

Frequency of SACS variants in 23andMe customers

<table>
<thead>
<tr>
<th>Variant name</th>
<th>European</th>
<th>African American</th>
<th>Ashkenazi Jewish</th>
<th>East Asian</th>
<th>Hispanic or Latino</th>
<th>South Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>6594delT</td>
<td>0.01%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
</tr>
</tbody>
</table>

This test is expected to detect 94% of carriers of French Canadian descent for this condition.

Pre-test and post-test carrier risks for the 23andMe PGS Carrier Status Test for ARSACS

<table>
<thead>
<tr>
<th></th>
<th>Carrier detection rate for this test</th>
<th>Pre-test (average) carrier risk</th>
<th>Post-test carrier risk for result “0 Variants Detected”</th>
</tr>
</thead>
<tbody>
<tr>
<td>French Canadian</td>
<td>94%</td>
<td>1 in 22</td>
<td>1 in 340</td>
</tr>
<tr>
<td>Other ethnicities*</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

*This condition is rare and not well studied in other ethnicities.
Accuracy

23andMe performed a method comparison study to assess the accuracy of the assay. Results of the test were compared with sequencing results for 67 samples with known variant status. Agreement between the two methods was >99% for all samples analyzed. The 95% confidence interval was 93.5% to 100%.

Precision/Reproducibility

A study was performed to assess the precision of the test. A total of 1,080 sample replicates were run across different testing conditions. This study yielded correct results for >99% of samples across all conditions tested. The study had >99% reproducibility and >99% repeatability.

References


Autosomal Recessive Polycystic Kidney Disease

Indications for Use

The 23andMe PGS Carrier Status Test for Autosomal Recessive Polycystic Kidney Disease (ARPKD) is indicated for the detection of 3 variants in the PKHD1 gene. This test is intended to be used to determine carrier status for ARPKD in adults, but cannot determine if a person has two copies of a tested variant.

Special considerations

- The test does not include a large fraction of variants that cause ARPKD in any ethnicity.
- There are currently no professional guidelines in the U.S. for carrier testing for ARPKD.
Clinical performance

The variants covered by this test are most common in people of Finnish descent. Worldwide, about 1 in 70 people is a carrier for ARPKD.

Frequency of PKHD1 variants in 23andMe customers

<table>
<thead>
<tr>
<th>Variant name</th>
<th>European</th>
<th>African American</th>
<th>Ashkenazi Jewish</th>
<th>East Asian</th>
<th>Hispanic or Latino</th>
<th>South Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>T36M</td>
<td>0.12%</td>
<td>0.04%</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
<td>0.05%</td>
<td>&lt;0.05%</td>
</tr>
<tr>
<td>R496X</td>
<td>0.01%</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>&lt;0.01%</td>
<td>&lt;0.05%</td>
</tr>
<tr>
<td>D3230fs</td>
<td>0.01%</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.08%</td>
<td>0.00%</td>
</tr>
</tbody>
</table>

This test is expected to detect about 66% of carriers of Finnish descent. The test does not cover variants causing the majority of ARPKD in people of general European, Hispanic, Middle Eastern, or Turkish descent.

Pre-test and post-test carrier risks for the 23andMe PGS Carrier Status Test for ARPKD

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Carrier detection rate for this test</th>
<th>Pre-test (average) carrier risk</th>
<th>Post-test carrier risk for result “0 Variants Detected”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finnish</td>
<td>66%</td>
<td>1 in 70</td>
<td>1 in 200</td>
</tr>
<tr>
<td>European</td>
<td>25%</td>
<td>1 in 70</td>
<td>1 in 93</td>
</tr>
<tr>
<td>Hispanic</td>
<td>22%</td>
<td>1 in 70</td>
<td>1 in 89</td>
</tr>
<tr>
<td>Middle Eastern</td>
<td>&lt;1%</td>
<td>1 in 70</td>
<td>1 in 70</td>
</tr>
<tr>
<td>Turkish</td>
<td>&lt;1%</td>
<td>1 in 70</td>
<td>1 in 70</td>
</tr>
<tr>
<td>Other ethnicities*</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

*This condition is not well studied in other ethnicities.

Accuracy

23andMe performed a method comparison study to assess the accuracy of the assay. Results of the test were compared with sequencing results for 149 samples with known variant status. Agreement between the two methods was >99% for all samples analyzed. The 95% confidence interval was 97.0% to 100%.

Precision/Reproducibility

A study was performed to assess the precision of the test. A total of 3,240 sample replicates were run across different testing conditions. This study yielded correct results for >99% of samples across all conditions tested. The study had >99% reproducibility and >99% repeatability.
Selected References


ARPKD Mutation Database. URL: http://www.humgen.rwth-aachen.de/

Additional references included in the report.

Beta Thalassemia and Related Hemoglobinopathies

Indications for Use

The 23andMe PGS Carrier Status Test for Beta Thalassemia and Related Hemoglobinopathies is indicated for the detection of 10 variants in the HBB gene. This test is intended to be used to determine carrier status for beta thalassemia and related hemoglobinopathies in adults, but cannot determine if a person has two copies of a tested variant. The test is most relevant for people of Cypriot, Greek, Italian (particularly Sicilian), and Sardinian descent.

Special considerations

- Symptoms of beta thalassemia may vary between people with the condition depending on the variants involved.
- Carrier testing for beta thalassemia and related hemoglobinopathies is recommended by ACOG for people of Mediterranean, African, and Southeast Asian descent considering having children. This test includes the variant recommended for testing by ACMG.

Clinical performance

The variants covered by this test are most common in people of Cypriot, Greek, Italian, Sicilian, Sardinian, Albanian, Macedonian, Bangladeshi, and Indonesian descent. This test does not cover a large fraction of HBB variants that cause beta thalassemia in people of Turkish, Croatian, Maharashtran, Azerbaijani, Pakistani, Pathan, Punjabi, Taiwanese, Malaysian, Singaporean, Thai, North African, and Middle Eastern descent. About 1 in 8 people (12.5%) of Cypriot descent, 1 in 10 people (10%) of Greek descent, up to 1 in 12 people (8.33%) of Italian (particularly from Sicily) descent, 1 in 9 people (11.11%) of Sardinian descent, and 1 in 23 people (4.35%) of Turkish descent are carriers for beta thalassemia.

Frequency of HBB variants in 23andMe customers

<table>
<thead>
<tr>
<th>Variant name</th>
<th>European</th>
<th>African American</th>
<th>Ashkenazi Jewish</th>
<th>East Asian</th>
<th>Hispanic or Latino</th>
<th>South Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>-29A&gt;G</td>
<td>0.00%</td>
<td>0.37%</td>
<td>0.00%</td>
<td>&lt;0.02%</td>
<td>0.01%</td>
<td>0.00%</td>
</tr>
<tr>
<td></td>
<td>Carrier detection rate for this test</td>
<td>Pre-test (average) carrier risk</td>
<td>Post-test carrier risk for result “0 Variants Detected”</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>--------------------</td>
<td>--------------------------------------</td>
<td>---------------------------------</td>
<td>-------------------------------------------------------</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Greek and Turkish Cypriot</td>
<td>90%</td>
<td>1 in 8</td>
<td>1 in 71</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Greek</td>
<td>75%</td>
<td>1 in 10</td>
<td>1 in 37</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Italian (particularly from Sicily)</td>
<td>82%</td>
<td>1 in 12</td>
<td>1 in 61</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sardinian</td>
<td>97%</td>
<td>1 in 9</td>
<td>1 in 250</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Turkish</td>
<td>66%</td>
<td>1 in 23</td>
<td>1 in 65</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Balkan</td>
<td>41-80%</td>
<td>Unknown</td>
<td>Unknown</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>South Asian</td>
<td>20-70%</td>
<td>Unknown</td>
<td>Unknown</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Southeast Asian</td>
<td>11-73%</td>
<td>Unknown</td>
<td>Unknown</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>North African</td>
<td>50-61%</td>
<td>Unknown</td>
<td>Unknown</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Middle Eastern</td>
<td>29-64%</td>
<td>Unknown</td>
<td>Unknown</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other ethnicities*</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*This condition is not as well studied in other ethnicities.

**Accuracy**

23andMe performed a method comparison study to assess the accuracy of the assay. Results of the test were compared with sequencing results for 461 samples with known variant status. Agreement between the two methods was >99% for all samples analyzed. The 95% confidence interval was 99.0% to 100%.
Precision/Reproducibility

A study was performed to assess the precision of the test. A total of 11,880 sample replicates were run across different testing conditions. This study yielded correct results for >99% of samples across all conditions tested. The study had >99% reproducibility and >99% repeatability.

References


Bloom Syndrome

Indications for Use

The 23andMe PGS Carrier Status Test for Bloom Syndrome is indicated for the detection of the BLMAsh variant in the BLM gene. This test is intended to be used to determine carrier status for Bloom syndrome in adults, but cannot determine if a person has two copies of a tested variant. The test is most relevant for people of Ashkenazi Jewish descent.

Special considerations

- Symptoms of Bloom syndrome may vary between people with the condition even if they have the same genetic variants.
• Carrier testing for Bloom syndrome is recommended by ACMG for people of Ashkenazi Jewish descent considering having children. This test includes the variant recommended for testing by ACMG.

Clinical performance

The variant covered by this test is most common in people of Ashkenazi Jewish descent. About 1 in 107 people (0.93%) of Ashkenazi Jewish descent carries this variant.

Frequency of BLM variants in 23andMe customers

<table>
<thead>
<tr>
<th>Variant name</th>
<th>European</th>
<th>African American</th>
<th>Ashkenazi Jewish</th>
<th>East Asian</th>
<th>Hispanic or Latino</th>
<th>South Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>BLM\textsuperscript{Ash}</td>
<td>0.02%</td>
<td>&lt; 0.01%</td>
<td>1.04%</td>
<td>0.00%</td>
<td>0.05%</td>
<td>0.00%</td>
</tr>
</tbody>
</table>

This test is expected to detect more than 99% of carriers of Ashkenazi Jewish descent for this condition.

Pre-test and post-test carrier risks for the 23andMe PGS Carrier Status Test for Bloom Syndrome

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Carrier detection rate for this test</th>
<th>Pre-test (average) carrier risk</th>
<th>Post-test carrier risk for result “0 Variants Detected”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ashkenazi Jewish</td>
<td>&gt; 99%</td>
<td>1 in 107</td>
<td>1 in 11,000</td>
</tr>
<tr>
<td>Other ethnicities*</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

*This condition is rare and not well studied in other ethnicities.

Accuracy

23andMe performed a method comparison study to assess the accuracy of the assay. The study was performed with 65 saliva samples, and 5 human cell-line samples. Results of the test were compared with sequencing results. Agreement between the two methods was >99% for all samples analyzed. The 95% confidence interval was 93.8% to 100%.

Precision/Reproducibility

A study was performed to assess the precision of the test. A total of 2,160 sample replicates were run across different testing conditions. This study yielded correct results for >99% of samples across all conditions tested. The study had >99% reproducibility and >99% repeatability.

Selected References

Congenital Disorder of Glycosylation Type 1a (PMM2-CDG)

Indications for Use

The 23andMe PGS Carrier Status Test for Congenital Disorder of Glycosylation Type 1a (PMM2-CDG) is indicated for the detection of 2 variants in the PMM2 gene. This test is intended to be used to determine carrier status for PMM2-CDG in adults, but cannot determine if a person has two copies of a tested variant. The test is most relevant for people of Danish descent.

Special considerations

- Severity of symptoms can vary in people with this disorder, even when the same variants are involved.
- There are currently no professional guidelines in the U.S. for carrier testing for this condition.

Clinical performance

The variants covered by this test are most common in people of Danish and Dutch descent. About 1 in 52 people (1.92%) of Danish descent and 1 in 62 people (1.61%) of Dutch descent are carriers for PMM2-CDG. This test does not include a large fraction of PMM2 variants that cause PMM2-CDG in people of Dutch descent.

Frequency of PMM2 variants in 23andMe customers

<table>
<thead>
<tr>
<th>Variant name</th>
<th>European</th>
<th>African American</th>
<th>Ashkenazi Jewish</th>
<th>East Asian</th>
<th>Hispanic or Latino</th>
<th>South Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>R141H</td>
<td>1.02%</td>
<td>0.33%</td>
<td>1.52%</td>
<td>&lt;0.02%</td>
<td>0.72%</td>
<td>0.05%</td>
</tr>
<tr>
<td>F119L</td>
<td>0.01%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
</tr>
</tbody>
</table>

This test is expected to detect 89% of carriers of Danish descent and 55% of carriers of Dutch descent for this condition.

Pre-test and post-test carrier risks for the 23andMe PGS Carrier Status Test for PMM2-CDG

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Carrier detection rate for this test</th>
<th>Pre-test (average) carrier risk</th>
<th>Post-test carrier risk for result “0 Variants Detected”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Danish</td>
<td>89%</td>
<td>1 in 52</td>
<td>1 in 450</td>
</tr>
<tr>
<td>Dutch</td>
<td>55%</td>
<td>1 in 62</td>
<td>1 in 137</td>
</tr>
<tr>
<td>Other ethnicities*</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

*This condition is not well studied in other ethnicities.
Accuracy

23andMe performed a method comparison study to assess the accuracy of the assay. Results of the test were compared with sequencing results for 100 samples with known variant status. Agreement between the two methods was >99% for all samples analyzed. The 95% confidence interval was 95.6% to 100%.

Precision/Reproducibility

A study was performed to assess the precision of the test. A total of 1,890 sample replicates were run across different testing conditions. This study yielded correct results for >99% of samples across all conditions tested. The study had >99% reproducibility and >99% repeatability.

Selected References


Additional references included in the report.

Cystic Fibrosis

Indications for Use

The 23andMe PGS Carrier Status Test for Cystic Fibrosis is indicated for the detection of 28 variants in the CFTR gene, including 21 of the 23 variants recommended for testing by ACMG. This test is intended to be used to determine carrier status for cystic fibrosis in adults, but cannot determine if a person has two copies of a tested variant. The test is most relevant for people of Ashkenazi Jewish, European, and Hispanic descent.

Special considerations

- Symptoms of cystic fibrosis may vary depending on the variants involved.
- ACMG recommends carrier testing for cystic fibrosis for people of all ethnicities considering having children. This test includes 21 of the 23 variants recommended for testing by ACMG.

Clinical performance

The variants covered by this test are found in people of all ethnicities. About 1 in 24 people (4.17%) of Ashkenazi Jewish descent, 1 in 25 people (4.00%) of European descent, 1 in 58 people (1.72%) of Hispanic or Latino descent, 1 in 61 people (1.64%) of
African American descent, and 1 in 94 people (1.06%) of Asian descent are carriers for cystic fibrosis.

Frequency of CFTR variants in 23andMe customers

<table>
<thead>
<tr>
<th>Variant name</th>
<th>European</th>
<th>African American</th>
<th>Ashkenazi Jewish</th>
<th>East Asian</th>
<th>Hispanic or Latino</th>
<th>South Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>DeltaF508</td>
<td>2.67%</td>
<td>0.88%</td>
<td>1.04%</td>
<td>0.00%</td>
<td>1.51%</td>
<td>0.52%</td>
</tr>
<tr>
<td>Delta507</td>
<td>0.01%</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.02%</td>
<td>0.00%</td>
</tr>
<tr>
<td>G85E</td>
<td>0.01%</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.01%</td>
<td>0.00%</td>
</tr>
<tr>
<td>R334W</td>
<td>0.01%</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
<td>&lt;0.02%</td>
<td>0.03%</td>
<td>0.00%</td>
</tr>
<tr>
<td>R347H</td>
<td>0.01%</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
<td>&lt;0.02%</td>
<td>0.01%</td>
<td>0.00%</td>
</tr>
<tr>
<td>R347P</td>
<td>0.01%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
</tr>
<tr>
<td>A455E</td>
<td>0.01%</td>
<td>0.00%</td>
<td>0.07%</td>
<td>&lt;0.02%</td>
<td>0.01%</td>
<td>0.00%</td>
</tr>
<tr>
<td>V520F</td>
<td>0.01%</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
</tr>
<tr>
<td>G542X</td>
<td>0.09%</td>
<td>0.04%</td>
<td>0.20%</td>
<td>0.00%</td>
<td>0.10%</td>
<td>0.00%</td>
</tr>
<tr>
<td>S549N</td>
<td>&lt;0.01%</td>
<td>0.02%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>&lt;0.01%</td>
<td>&lt;0.05%</td>
</tr>
<tr>
<td>G551D</td>
<td>0.08%</td>
<td>0.02%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.03%</td>
<td>0.00%</td>
</tr>
<tr>
<td>R553X</td>
<td>0.04%</td>
<td>0.03%</td>
<td>0.00%</td>
<td>&lt;0.02%</td>
<td>0.02%</td>
<td>0.00%</td>
</tr>
<tr>
<td>R560T</td>
<td>0.01%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
</tr>
<tr>
<td>R1162X</td>
<td>0.01%</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.02%</td>
<td>&lt;0.05%</td>
</tr>
<tr>
<td>W1282X</td>
<td>0.06%</td>
<td>0.02%</td>
<td>1.93%</td>
<td>0.00%</td>
<td>0.03%</td>
<td>0.00%</td>
</tr>
<tr>
<td>N1303K</td>
<td>0.05%</td>
<td>0.01%</td>
<td>0.16%</td>
<td>0.00%</td>
<td>0.05%</td>
<td>0.00%</td>
</tr>
<tr>
<td>394delTT</td>
<td>0.01%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
</tr>
<tr>
<td>621+1G&gt;T</td>
<td>0.04%</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.02%</td>
<td>0.00%</td>
</tr>
<tr>
<td>711+1G&gt;T</td>
<td>0.01%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>&lt;0.02%</td>
<td>0.01%</td>
<td>0.00%</td>
</tr>
<tr>
<td>1078delT</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.01%</td>
<td>0.00%</td>
</tr>
<tr>
<td>1717-1G&gt;A</td>
<td>0.04%</td>
<td>&lt;0.01%</td>
<td>0.05%</td>
<td>&lt;0.02%</td>
<td>0.02%</td>
<td>0.00%</td>
</tr>
<tr>
<td>1898+1G&gt;A</td>
<td>0.01%</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>&lt;0.01%</td>
<td>&lt;0.05%</td>
</tr>
<tr>
<td>3120+1G&gt;A</td>
<td>&lt;0.01%</td>
<td>0.19%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.02%</td>
<td>0.00%</td>
</tr>
<tr>
<td>3659delC</td>
<td>0.03%</td>
<td>&lt;0.01%</td>
<td>&lt;0.01%</td>
<td>&lt;0.02%</td>
<td>0.02%</td>
<td>&lt;0.05%</td>
</tr>
<tr>
<td>3905insT</td>
<td>0.01%</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
</tr>
<tr>
<td>3849+10kbC&gt;T</td>
<td>0.03%</td>
<td>&lt;0.01%</td>
<td>0.21%</td>
<td>0.00%</td>
<td>0.04%</td>
<td>0.05%</td>
</tr>
<tr>
<td>2184delA</td>
<td>0.01%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.02%</td>
<td>0.01%</td>
<td>0.00%</td>
</tr>
<tr>
<td>3876delA</td>
<td>0.00%</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.01%</td>
<td>0.00%</td>
</tr>
</tbody>
</table>

This test is expected to detect 95% of carriers of Ashkenazi Jewish descent, 89% of carriers of European descent, 73% of carriers of Hispanic descent, 65% of carriers of African American descent, and 55% of carriers of Asian descent for this condition.
Pre-test and post-test carrier risks for the 23andMe PGS Carrier Status Test for Cystic Fibrosis

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Carrier detection rate for this test</th>
<th>Pre-test (average) carrier risk</th>
<th>Post-test carrier risk for result “0 Variants Detected”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ashkenazi Jewish</td>
<td>95%</td>
<td>1 in 24</td>
<td>1 in 420</td>
</tr>
<tr>
<td>European</td>
<td>89%</td>
<td>1 in 25</td>
<td>1 in 220</td>
</tr>
<tr>
<td>Hispanic</td>
<td>73%</td>
<td>1 in 58</td>
<td>1 in 210</td>
</tr>
<tr>
<td>African American</td>
<td>65%</td>
<td>1 in 61</td>
<td>1 in 173</td>
</tr>
<tr>
<td>Asian</td>
<td>55%</td>
<td>1 in 94</td>
<td>1 in 210</td>
</tr>
<tr>
<td>Other ethnicities*</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

*This condition is not as well studied in other ethnicities.

**Accuracy**

23andMe performed a method comparison study to assess the accuracy of the assay. Results of the test were compared with sequencing results for 1514 samples with known variant status. Agreement between the two methods was >99% for all samples analyzed. The 95% confidence interval was 99.6% to 100%.

**Precision/Reproducibility**

A study was performed to assess the precision of the test. A total of 31,050 sample replicates were run across different testing conditions. This study yielded correct results for >99% of samples across all conditions tested. The study had >99% reproducibility and >99% repeatability.

**References**


D-Bifunctional Protein Deficiency

Indications for Use

The 23andMe PGS Carrier Status Test for D-Bifunctional Protein Deficiency (DBPD) is indicated for the detection of 2 variants in the HSD17B4 gene. This test is intended to be used to determine carrier status for DBPD in adults, but cannot determine if a person has two copies of a tested variant.

Special considerations

- This test does not include the majority of HSD17B4 variants that cause DBPD in any ethnicity.
- There are currently no professional guidelines in the U.S. for carrier testing for this condition.

Clinical performance

The variants covered by this test are rare in all ethnicities.

Frequency of HSD17B4 variants in 23andMe customers

<table>
<thead>
<tr>
<th>Variant name</th>
<th>European</th>
<th>African American</th>
<th>Ashkenazi Jewish</th>
<th>East Asian</th>
<th>Hispanic or Latino</th>
<th>South Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>G16S</td>
<td>0.09%</td>
<td>0.01%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.03%</td>
<td>0.00%</td>
</tr>
<tr>
<td>N457Y</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.04%</td>
<td>0.00%</td>
</tr>
</tbody>
</table>

This test is expected to detect 35% of carriers for this condition.

Pre-test and post-test carrier risks for the 23andMe PGS Carrier Status Test for DBPD

<table>
<thead>
<tr>
<th>All ethnicities*</th>
<th>Carrier detection rate for this test</th>
<th>Pre-test (average) carrier risk</th>
<th>Post-test carrier risk for result “0 Variants Detected”</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>35%</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

*This condition is not well studied in any ethnicity.

Accuracy

23andMe performed a method comparison study to assess the accuracy of the assay. Results of the test were compared with sequencing results for 97 samples with known variant status. Agreement between the two methods was >99% for all samples analyzed. The 95% confidence interval was 95.6% to 100%.
Precision/Reproducibility

A study was performed to assess the precision of the test. A total of 1,620 sample replicates were run across different testing conditions. This study yielded correct results for >99% of samples across all conditions tested. The study had >99% reproducibility and >99% repeatability.

Selected References


Additional references included in the report.

Dihydrolipoamide Dehydrogenase Deficiency

Indications for Use

The 23andMe PGS Carrier Status Test for Dihydrolipoamide Dehydrogenase (DLD) Deficiency is indicated for the detection of the G229C variant in the DLD gene. This test is intended to be used to determine carrier status for DLD deficiency in adults, but cannot determine if a person has two copies of a tested variant. The test is most relevant for people of Ashkenazi Jewish descent.

Special considerations

- There are currently no professional guidelines in the U.S. for carrier testing for this condition.

Clinical performance

The variant covered by this test is most common in people of Ashkenazi Jewish descent. About 1 in 107 people (0.93%) of Ashkenazi Jewish descent is a carrier for DLD deficiency.

Frequency of DLD variants in 23andMe customers

<table>
<thead>
<tr>
<th>Variant name</th>
<th>European</th>
<th>African American</th>
<th>Ashkenazi Jewish</th>
<th>East Asian</th>
<th>Hispanic or Latino</th>
<th>South Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>G229C</td>
<td>0.03%</td>
<td>&lt;0.01%</td>
<td>1.15%</td>
<td>0.00%</td>
<td>0.01%</td>
<td>&lt;0.05%</td>
</tr>
</tbody>
</table>

This test is expected to detect 86% of carriers of Ashkenazi Jewish descent for this condition.
Pre-test and post-test carrier risks for the 23andMe PGS Carrier Status Test for DLD Deficiency

<table>
<thead>
<tr>
<th></th>
<th>Carrier detection rate for this test</th>
<th>Pre-test (average) carrier risk</th>
<th>Post-test carrier risk for result “0 Variants Detected”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ashkenazi Jewish</td>
<td>86%</td>
<td>1 in 107</td>
<td>1 in 740</td>
</tr>
<tr>
<td>Other ethnicities*</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

*This condition is not well studied in other ethnicities.

**Accuracy**

23andMe performed a method comparison study to assess the accuracy of the assay. Results of the test were compared with sequencing results for 50 samples with known variant status. Agreement between the two methods was >99% for all samples analyzed. The 95% confidence interval was 91.5% to 100%.

**Precision/Reproducibility**

A study was performed to assess the precision of the test. A total of 1,080 sample replicates were run across different testing conditions. This study yielded correct results for >99% of samples across all conditions tested. The study had >99% reproducibility and >99% repeatability.

**Selected References**


Additional references included in the report.

**Familial Dysautonomia**

*Indications for Use*

The 23andMe PGS Carrier Status Test for Familial Dysautonomia is indicated for the detection of the 2507+6T>C variant in the IKBKAP gene. This test is intended to be used to determine carrier status for familial dysautonomia in adults, but cannot determine if a person has two copies of a tested variant. The test is most relevant for people of Ashkenazi Jewish descent.
Special considerations

- Carrier testing for familial dysautonomia is recommended by ACMG for people of Ashkenazi Jewish descent considering having children. This test includes 1 of 2 variants recommended for testing by ACMG.

Clinical performance

The variant covered by this test is most common in people of Ashkenazi Jewish descent. About 1 in 31 people (3.23%) of Ashkenazi Jewish descent is a carrier for familial dysautonomia.

Frequency of IKBKAP variants in 23andMe customers

<table>
<thead>
<tr>
<th>Variant name</th>
<th>European</th>
<th>African American</th>
<th>Ashkenazi Jewish</th>
<th>East Asian</th>
<th>Hispanic or Latino</th>
<th>South Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>2507+6T&gt;C</td>
<td>0.07%</td>
<td>0.03%</td>
<td>3.22%</td>
<td>0.00%</td>
<td>0.05%</td>
<td>0.00%</td>
</tr>
</tbody>
</table>

This test is expected to detect about 99% of carriers of Ashkenazi Jewish descent for this condition.

Pre-test and post-test carrier risks for the 23andMe PGS Carrier Status Test for Familial Dysautonomia

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Carrier detection rate for this test</th>
<th>Pre-test (average) carrier risk</th>
<th>Post-test carrier risk for result “0 Variants Detected”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ashkenazi Jewish</td>
<td>99%</td>
<td>1 in 31</td>
<td>1 in 2,300</td>
</tr>
<tr>
<td>Other ethnicities*</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

*This condition is not as well studied in other ethnicities.

Accuracy

23andMe performed a method comparison study to assess the accuracy of the assay. Results of the test were compared with sequencing results for 59 samples with known variant status. Agreement between the two methods was >99% for all samples analyzed. The 95% confidence interval was 92.9% to 100%.

Precision/Reproducibility

A study was performed to assess the precision of the test. A total of 1,080 sample replicates were run across different testing conditions. This study yielded correct results for >99% of samples across all conditions tested. The study had >99% reproducibility and >99% repeatability.
Selected References


Additional references included in the report.

Fanconi Anemia Group C

Indications for Use

The 23andMe PGS Carrier Status Test for Fanconi Anemia Group C is indicated for the detection of 3 variants in the FANCC gene. This test is intended to be used to determine carrier status for Fanconi anemia group C in adults, but cannot determine if a person has two copies of a tested variant. The test is most relevant for people of Ashkenazi Jewish descent.

Special considerations

- Carrier testing for Fanconi anemia group C is recommended by ACMG for people of Ashkenazi Jewish descent considering having children. This test includes the 1 variant recommended for testing by ACMG.

Clinical performance

The variants covered by this test are most common in people of Ashkenazi Jewish descent. About 1 in 89 people (1.12%) of Ashkenazi Jewish descent is a carrier for Fanconi anemia group C.

Frequency of FANCC variants in 23andMe customers

<table>
<thead>
<tr>
<th>Variant name</th>
<th>European</th>
<th>African American</th>
<th>Ashkenazi Jewish</th>
<th>East Asian</th>
<th>Hispanic or Latino</th>
<th>South Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVS4+4A&gt;T</td>
<td>0.03%</td>
<td>0.02%</td>
<td>1.18%</td>
<td>0.00%</td>
<td>0.02%</td>
<td>0.00%</td>
</tr>
<tr>
<td>R548X</td>
<td>0.03%</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.02%</td>
<td>0.00%</td>
</tr>
<tr>
<td>322delG</td>
<td>0.04%</td>
<td>0.01%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.01%</td>
<td>0.00%</td>
</tr>
</tbody>
</table>

This test is expected to detect more than 99% of carriers of Ashkenazi Jewish descent for this condition.
Pre-test and post-test carrier risks for the 23andMe PGS Carrier Status Test for Fanconi Anemia Group C

<table>
<thead>
<tr>
<th></th>
<th>Carrier detection rate for this test</th>
<th>Pre-test (average) carrier risk</th>
<th>Post-test carrier risk for result “0 Variants Detected”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ashkenazi Jewish</td>
<td>&gt;99%</td>
<td>1 in 89</td>
<td>1 in 88,000</td>
</tr>
<tr>
<td>Other ethnicities*</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

*This condition is not as well studied in other ethnicities.

**Accuracy**

23andMe performed a method comparison study to assess the accuracy of the assay. Results of the test were compared with sequencing results for 145 samples with known variant status. Agreement between the two methods was >99% for all samples analyzed. The 95% confidence interval was 97.0% to 100%.

**Precision/Reproducibility**

A study was performed to assess the precision of the test. A total of 3,240 sample replicates were run across different testing conditions. This study yielded correct results for >99% of samples across all conditions tested. The study had >99% reproducibility and >99% repeatability.

**References**


Additional references included in the report.

**Glycogen Storage Disease Type Ia**

**Indications for Use**

The 23andMe PGS Carrier Status Test for Glycogen Storage Disease Type Ia (GSDIa) is indicated for the detection of the R83C variant in the G6PC gene. This test is intended to be used to determine carrier status for GSDIa in adults, but cannot determine if a person has two copies of a tested variant. The test is most relevant for people of Ashkenazi Jewish descent.

**Special considerations**
• There are currently no professional guidelines in the U.S. for carrier testing for this condition.

Clinical performance

The variant covered by this test is most common in people of Ashkenazi Jewish descent. About 1 in 70 people (1.43%) of Ashkenazi Jewish descent is a carrier for GSDIa.

Frequency of G6PC variants in 23andMe customers

<table>
<thead>
<tr>
<th>Variant name</th>
<th>European</th>
<th>African American</th>
<th>Ashkenazi Jewish</th>
<th>East Asian</th>
<th>Hispanic or Latino</th>
<th>South Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>R83C</td>
<td>0.11%</td>
<td>0.03%</td>
<td>1.40%</td>
<td>&lt;0.02%</td>
<td>0.12%</td>
<td>&lt;0.05%</td>
</tr>
</tbody>
</table>

This test is expected to detect 98% of carriers of Ashkenazi Jewish descent for this condition.

Pre-test and post-test carrier risks for the 23andMe PGS Carrier Status Test for GSDIa

<table>
<thead>
<tr>
<th>Ashkenazi Jewish</th>
<th>Carrier detection rate for this test</th>
<th>Pre-test (average) carrier risk</th>
<th>Post-test carrier risk for result “0 Variants Detected”</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>98%</td>
<td>1 in 70</td>
<td>1 in 3,200</td>
</tr>
<tr>
<td>Other ethnicities*</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

*This condition is not as well studied in other ethnicities.

Accuracy

23andMe performed a method comparison study to assess the accuracy of the assay. Results of the test were compared with sequencing results for 49 samples with known variant status. Agreement between the two methods was >99% for all samples analyzed. The 95% confidence interval was 91.3% to 100%.

Precision/Reproducibility

A study was performed to assess the precision of the test. A total of 1,350 sample replicates were run across different testing conditions. This study yielded correct results for >99% of samples across all conditions tested. The study had >99% reproducibility and >99% repeatability.

Selected References

Chou JY et al. (2008). "Mutations in the glucose-6-phosphatase-alpha (G6PC) gene that cause type Ia glycogen storage disease." Hum Mutat. 29(7):921-30.

Additional references included in the report.

Glycogen Storage Disease Type Ib

*Indications for Use*

The 23andMe PGS Carrier Status Test for Glycogen Storage Disease Type Ib (GSDIb) is indicated for the detection of 2 variants in the SLC37A4 gene. This test is intended to be used to determine carrier status for GSDIb in adults, but cannot determine if a person has two copies of a tested variant.

*Special considerations*

- This test does not include the majority of SLC37A4 variants that cause GSDIb in any ethnicity.
- There are currently no professional guidelines in the U.S. for carrier testing for this condition.

*Clinical performance*

The variants covered by this test are rare in all ethnicities.

Frequency of SLC37A4 variants in 23andMe customers

<table>
<thead>
<tr>
<th>Variant name</th>
<th>European</th>
<th>African American</th>
<th>Ashkenazi Jewish</th>
<th>East Asian</th>
<th>Hispanic or Latino</th>
<th>South Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>1042_1043delCT</td>
<td>0.06%</td>
<td>0.03%</td>
<td>0.02%</td>
<td>0.03%</td>
<td>0.06%</td>
<td>0.00%</td>
</tr>
<tr>
<td>W118R</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>&lt;0.02%</td>
<td>0.00%</td>
<td>0.00%</td>
</tr>
</tbody>
</table>

This test is expected to detect 42% of carriers of Japanese descent and 31% of carriers of European descent for this condition.

Pre-test and post-test carrier risks for the 23andMe PGS Carrier Status Test for GSDIb

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Carrier detection rate for this test</th>
<th>Pre-test (average) carrier risk</th>
<th>Post-test carrier risk for result “0 Variants Detected”</th>
</tr>
</thead>
<tbody>
<tr>
<td>European</td>
<td>31%</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>Japanese</td>
<td>42%</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>Other ethnicities*</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

*This condition is not as well studied in other ethnicities.*
Accuracy

23andMe performed a method comparison study to assess the accuracy of the assay. Results of the test were compared with sequencing results for 85 samples with known variant status. Agreement between the two methods was >99% for all samples analyzed. The 95% confidence interval was 94.9% to 100%.

Precision/Reproducibility

A study was performed to assess the precision of the test. A total of 2,160 sample replicates were run across different testing conditions. This study yielded correct results for >99% of samples across all conditions tested. The study had >99% reproducibility and >99% repeatability.

Selected References


Additional references included in the report.

GRACILE Syndrome

Indications for Use

The 23andMe PGS Carrier Status Test for GRACILE Syndrome is indicated for the detection of the S78G variant in the BCS1L gene. This test is intended to be used to determine carrier status for GRACILE Syndrome in adults, but cannot determine if a person has two copies of a tested variant. The test is most relevant for people of Finnish descent.

Special considerations

• There are currently no professional guidelines in the U.S. for carrier testing for this condition.

Clinical performance

The variant covered by this test is most common in people of Finnish descent. About 1 in 110 people (0.91%) of Finnish descent is a carrier for GRACILE syndrome.

Frequency of BCS1L variants in 23andMe customers

<table>
<thead>
<tr>
<th>Variant name</th>
<th>European</th>
<th>African American</th>
<th>Ashkenazi Jewish</th>
<th>East Asian</th>
<th>Hispanic or Latino</th>
<th>South Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>S78G</td>
<td>0.03%</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.02%</td>
<td>0.00%</td>
</tr>
</tbody>
</table>
This test is expected to detect more than 99% of carriers of Finnish descent for this condition.

Pre-test and post-test carrier risks for the 23andMe PGS Carrier Status Test for GRACILE Syndrome

<table>
<thead>
<tr>
<th></th>
<th>Carrier detection rate for this test</th>
<th>Pre-test (average) carrier risk</th>
<th>Post-test carrier risk for result “0 Variants Detected”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finnish</td>
<td>&gt;99%</td>
<td>1 in 110</td>
<td>1 in 1,100,000</td>
</tr>
<tr>
<td>Other ethnicities*</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

*This condition is not as well studied in other ethnicities.

**Accuracy**

23andMe performed a method comparison study to assess the accuracy of the assay. Results of the test were compared with sequencing results for 46 samples with known variant status. Agreement between the two methods was >99% for all samples analyzed. The 95% confidence interval was 91.3% to 100%.

**Precision/Reproducibility**

A study was performed to assess the precision of the test. A total of 1,080 sample replicates were run across different testing conditions. This study yielded correct results for >99% of samples across all conditions tested. The study had >99% reproducibility and >99% repeatability.

**References**


Visapää I et al. (2002). "GRACILE syndrome, a lethal metabolic disorder with iron overload, is caused by a point mutation in BCS1L." Am J Hum Genet. 71(4):863-76.

**Hereditary Fructose Intolerance**

**Indications for Use**

The 23andMe PGS Carrier Status Test for Hereditary Fructose Intolerance is indicated for the detection of 4 variants in the ALDOB gene. This test is intended to be used to
determine carrier status for hereditary fructose intolerance in adults, but cannot determine if a person has two copies of a tested variant. The test is most relevant for people of European descent.

Special considerations

- There are currently no professional guidelines in the U.S. for carrier testing for this condition.

Clinical performance

The variants covered by this test are most common in people of European, Middle Eastern, and Turkish descent. About 1 in 71 people (1.41%) worldwide is a carrier for hereditary fructose intolerance.

Frequency of ALDOB variants in 23andMe customers

<table>
<thead>
<tr>
<th>Variant name</th>
<th>European</th>
<th>African American</th>
<th>Ashkenazi Jewish</th>
<th>East Asian</th>
<th>Hispanic or Latino</th>
<th>South Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>A149P</td>
<td>0.90%</td>
<td>0.30%</td>
<td>0.44%</td>
<td>0.00%</td>
<td>0.70%</td>
<td>&lt;0.05%</td>
</tr>
<tr>
<td>N335K</td>
<td>0.04%</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
<td>&lt;0.02%</td>
<td>0.03%</td>
<td>0.00%</td>
</tr>
<tr>
<td>Delta4E4</td>
<td>0.01%</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
<td>0.03%</td>
<td>0.04%</td>
<td>&lt;0.05%</td>
</tr>
</tbody>
</table>

This test is expected to detect 70% of carriers of European descent for this condition.

Pre-test and post-test carrier risks for the 23andMe PGS Carrier Status Test for Hereditary Fructose Intolerance

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Carrier detection rate for this test</th>
<th>Pre-test (average) carrier risk</th>
<th>Post-test carrier risk for result “0 Variants Detected”</th>
</tr>
</thead>
<tbody>
<tr>
<td>European</td>
<td>70%</td>
<td>1 in 71</td>
<td>1 in 240</td>
</tr>
<tr>
<td>Other ethnicities*</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

*This condition is not as well studied in other ethnicities.

Accuracy

23andMe performed a method comparison study to assess the accuracy of the assay. Results of the test were compared with sequencing results for 149 samples with known variant status. Agreement between the two methods was >99% for all samples analyzed. The 95% confidence interval was 97.0% to 100%.

Precision/Reproducibility

A study was performed to assess the precision of the test. A total of 3,240 sample replicates were run across different testing conditions. This study yielded correct results
for >99% of samples across all conditions tested. The study had >99% reproducibility and >99% repeatability.

Selected References


Additional references included in the report.

Leigh Syndrome, French-Canadian Type (LSFC)

Indications for Use

The 23andMe PGS Carrier Status Test for Leigh Syndrome, French Canadian Type (LSFC) is indicated for the detection of the A354V variant in the LRPPRC gene. This test is intended to be used to determine carrier status for LSFC in adults, but cannot determine if a person has two copies of a tested variant. The test is most relevant for people of French Canadian descent.

Special considerations

- There are currently no professional guidelines in the U.S. for carrier testing for this condition.

Clinical performance

The variant covered by this test is most common in people of French Canadian descent. About 1 in 23 people (4.35%) of French Canadian descent from the Saguenay-Lac-St. Jean region of Quebec is a carrier for LSFC.

Frequency of LRPPRC variants in 23andMe customers

<table>
<thead>
<tr>
<th>Variant name</th>
<th>European</th>
<th>African American</th>
<th>Ashkenazi Jewish</th>
<th>East Asian</th>
<th>Hispanic or Latino</th>
<th>South Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>A354V</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.01%</td>
<td>0.00%</td>
</tr>
</tbody>
</table>

This test is expected to detect more than 99% of carriers of French Canadian descent for this condition.
Pre-test and post-test carrier risks for the 23andMe PGS Carrier Status Test for LSFC

<table>
<thead>
<tr>
<th>Carrier detection rate for this test</th>
<th>Pre-test (average) carrier risk</th>
<th>Post-test carrier risk for result “0 Variants Detected”</th>
</tr>
</thead>
<tbody>
<tr>
<td>French Canadian</td>
<td>&gt;99%</td>
<td>1 in 23</td>
</tr>
<tr>
<td>Other ethnicities*</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>Unknown</td>
<td>1 in 2,500</td>
<td>1 in 2,500</td>
</tr>
</tbody>
</table>

*This condition is not well studied in other ethnicities.

**Accuracy**

23andMe performed a method comparison study to assess the accuracy of the assay. Results of the test were compared with sequencing results for 45 samples with known variant status. Agreement between the two methods was >99% for all samples analyzed. The 95% confidence interval was 90.8% to 100%.

**Precision/Reproducibility**

A study was performed to assess the precision of the test. A total of 1,080 sample replicates were run across different testing conditions. This study yielded correct results for >99% of samples across all conditions tested. The study had >99% reproducibility and >99% repeatability.

**Selected References**


Additional references included in the report.

**Limb-Girdle Muscular Dystrophy Type 2D**

**Indications for Use**

The 23andMe PGS Carrier Status Test for Limb-Girdle Muscular Dystrophy Type 2D (LGMD2D) is indicated for the detection of the R77C variant in the SGCA gene. This test is intended to be used to determine carrier status for LGMD2D in adults, but cannot determine if a person has two copies of a tested variant. The test is most relevant for people of Finnish descent.
Special considerations

- Symptoms can vary greatly in people with this condition, and can be mild in some cases.
- There are currently no professional guidelines in the U.S. for carrier testing for this condition.

Clinical performance

The variant covered by this test is most common in people of Finnish descent. About 1 in 250 people (0.4%) of Finnish descent is a carrier for LGMD2D.

Frequency of SGCA variants in 23andMe customers

<table>
<thead>
<tr>
<th>Variant name</th>
<th>European</th>
<th>African American</th>
<th>Ashkenazi Jewish</th>
<th>East Asian</th>
<th>Hispanic or Latino</th>
<th>South Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>R77C</td>
<td>0.10%</td>
<td>0.03%</td>
<td>0.00%</td>
<td>&lt;0.02%</td>
<td>0.05%</td>
<td>0.00%</td>
</tr>
</tbody>
</table>

This test is expected to detect 95% of carriers of Finnish descent for this condition.

Pre-test and post-test carrier risks for the 23andMe PGS Carrier Status Test for LGMD2D

<table>
<thead>
<tr>
<th></th>
<th>Carrier detection rate for this test</th>
<th>Pre-test (average) carrier risk</th>
<th>Post-test carrier risk for result “0 Variants Detected”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finnish</td>
<td>95%</td>
<td>1 in 250</td>
<td>1 in 5,500</td>
</tr>
<tr>
<td>Other ethnicities*</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

*This condition is not as well studied in other ethnicities.

Accuracy

23andMe performed a method comparison study to assess the accuracy of the assay. Results of the test were compared with sequencing results for 49 samples with known variant status. Agreement between the two methods was >99% for all samples analyzed. The 95% confidence interval was 91.5% to 100%.

Precision/Reproducibility

A study was performed to assess the precision of the test. A total of 1,080 sample replicates were run across different testing conditions. This study yielded correct results for >99% of samples across all conditions tested. The study had >99% reproducibility and >99% repeatability.
Selected References


Additional references included in the report.

Limb-Girdle Muscular Dystrophy 2E

Indications for Use

The 23andMe PGS Carrier Status Test for Limb-Girdle Muscular Dystrophy Type 2E (LGMD2E) is indicated for the detection of the T151R variant in the SGCB gene. This test is intended to be used to determine carrier status for LGMD2E in adults, but cannot determine if a person has two copies of a tested variant. The test is most relevant for people of Amish descent.

Special considerations

- Symptoms can vary greatly in people with this condition, and can be mild in some cases.
- There are currently no professional guidelines in the U.S. for carrier testing for this condition.

Clinical performance

The variant covered by this test is most common in people of Southern Indiana Amish descent, though carrier frequency in this population is not known.

Frequency of SGCB variants in 23andMe customers

<table>
<thead>
<tr>
<th>Variant name</th>
<th>European</th>
<th>African American</th>
<th>Ashkenazi Jewish</th>
<th>East Asian</th>
<th>Hispanic or Latino</th>
<th>South Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>T151R</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
</tr>
</tbody>
</table>

This test is expected to detect more than 99% of carriers of Amish descent for this condition.

Pre-test and post-test carrier risks for the 23andMe PGS Carrier Status Test for LGMD2E

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Carrier detection rate for this test</th>
<th>Pre-test (average) carrier risk</th>
<th>Post-test carrier risk for result “0 Variants Detected”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amish from southern Indiana</td>
<td>&gt; 99%</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>Other ethnicities*</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

*This condition is not as well studied in other ethnicities.
Accuracy

23andMe performed a method comparison study to assess the accuracy of the assay. Results of the test were compared with sequencing results for 28 samples with known variant status. Agreement between the two methods was >99% for all samples analyzed. The 95% confidence interval was 85.7% to 100%.

Precision/Reproducibility

A study was performed to assess the precision of the test. A total of 1,080 sample replicates were run across different testing conditions. This study yielded correct results for >99% of samples across all conditions tested. The study had >99% reproducibility and >99% repeatability.

Selected References


Additional references included in the report.

Limb-Girdle Muscular Dystrophy 2I

Indications For Use

The 23andMe PGS Carrier Status Test for Limb-Girdle Muscular Dystrophy Type 2I (LGMD2I) is indicated for the detection of the L276I variant in the FKRP gene. This test is intended to be used to determine carrier status for LGMD2I in adults, but cannot determine if a person has two copies of a tested variant.

Special considerations

• Symptoms can vary greatly in people with this condition, and can be mild in some cases.
• There are currently no professional guidelines in the U.S. for carrier testing for this condition.

Clinical performance

The variant covered by this test is most common in people of European descent. About 1 in 200 people (0.5%) of European descent is a carrier for LGMD2I.
Frequency of FKRP variants in 23andMe customers

<table>
<thead>
<tr>
<th>Variant name</th>
<th>European</th>
<th>African American</th>
<th>Ashkenazi Jewish</th>
<th>East Asian</th>
<th>Hispanic or Latino</th>
<th>South Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>L276I</td>
<td>0.39%</td>
<td>0.08%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.15%</td>
<td>0.00%</td>
</tr>
</tbody>
</table>

This test is expected to detect 62% of carriers of European descent for this condition.

Pre-test and post-test carrier risks for the 23andMe PGS Carrier Status Test for LGMD2I

<table>
<thead>
<tr>
<th></th>
<th>Carrier detection rate for this test</th>
<th>Pre-test (average) carrier risk</th>
<th>Post-test carrier risk for result “0 Variants Detected”</th>
</tr>
</thead>
<tbody>
<tr>
<td>European</td>
<td>62%</td>
<td>1 in 200</td>
<td>1 in 520</td>
</tr>
<tr>
<td>Other ethnicities*</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

*This condition is not as well studied in other ethnicities.

**Accuracy**

23andMe performed a method comparison study to assess the accuracy of the assay. Results of the test were compared with sequencing results for 51 samples with known variant status. Agreement between the two methods was >99% for all samples analyzed. The 95% confidence interval was 91.6% to 100%.

**Precision/Reproducibility**

A study was performed to assess the precision of the test. A total of 1,080 sample replicates were run across different testing conditions. This study yielded correct results for >99% of samples across all conditions tested. The study had >99% reproducibility and >99% repeatability.

**Selected References**


Additional references included in the report.
Maple Syrup Urine Disease (MSUD) Type 1B

Indications for Use

The 23andMe PGS Carrier Status Test for Maple Syrup Urine Disease Type 1B (MSUD 1B) is indicated for the detection of 2 variants in the BCKDHB gene. This test is intended to be used to determine carrier status for MSUD 1B in adults, but cannot determine if a person has two copies of a tested variant. The test is most relevant for people of Ashkenazi Jewish descent.

Special considerations

• There are currently no professional guidelines in the U.S. for carrier testing for this condition.

Clinical performance

The variants covered by this test are most common in people of Ashkenazi Jewish descent. About 1 in 97 people (1.03%) of Ashkenazi Jewish descent is a carrier for MSUD 1B.

Frequency of BCKDHB variants in 23andMe customers

<table>
<thead>
<tr>
<th>Variant name</th>
<th>European</th>
<th>African American</th>
<th>Ashkenazi Jewish</th>
<th>East Asian</th>
<th>Hispanic or Latino</th>
<th>South Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>R183P</td>
<td>0.01%</td>
<td>&lt;0.01%</td>
<td>0.66%</td>
<td>&lt;0.02%</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
</tr>
<tr>
<td>G278S</td>
<td>0.08%</td>
<td>&lt;0.01%</td>
<td>0.26%</td>
<td>0.00%</td>
<td>0.03%</td>
<td>0.00%</td>
</tr>
</tbody>
</table>

This test is expected to detect 92% of carriers of Ashkenazi Jewish descent for this condition.

Pre-test and post-test carrier risks for the 23andMe PGS Carrier Status Test for MSUD 1B

<table>
<thead>
<tr>
<th></th>
<th>Carrier detection rate for this test</th>
<th>Pre-test (average) carrier risk</th>
<th>Post-test carrier risk for result “0 Variants Detected”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ashkenazi Jewish</td>
<td>92%</td>
<td>1 in 97</td>
<td>1 in 1,200</td>
</tr>
<tr>
<td>Other ethnicities*</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

*This condition is not as well studied in other ethnicities.

Accuracy

23andMe performed a method comparison study to assess the accuracy of the assay. Results of the test were compared with sequencing results for 92 samples with known variant status. Agreement between the two methods was >99% for all samples analyzed. The 95% confidence interval was 95.4% to 100%.
**Precision/Reproducibility**

A study was performed to assess the precision of the test. A total of 2,160 sample replicates were run across different testing conditions. This study yielded correct results for >99% of samples across all conditions tested. The study had >99% reproducibility and >99% repeatability.

**Selected References**


Additional references included in the report.

**MCAD Deficiency**

**Indications for Use**

The 23andMe PGS Carrier Status Test for Medium-Chain Acyl-CoA Dehydrogenase (MCAD) Deficiency is indicated for the detection of 3 variants in the ACADM gene. This test is intended to be used to determine carrier status for MCAD deficiency in adults, but cannot determine if a person has two copies of a tested variant. The test is most relevant for people of Northern European descent.

**Special considerations**

- There are currently no professional guidelines in the U.S. for carrier testing for this condition.

**Clinical performance**

The variants covered by this test are most common in people of European descent. About 1 in 100 people (1.00%) of European descent is a carrier for MCAD deficiency.

**Frequency of ACADM variants in 23andMe customers**

<table>
<thead>
<tr>
<th>Variant name</th>
<th>European</th>
<th>African American</th>
<th>Ashkenazi Jewish</th>
<th>East Asian</th>
<th>Hispanic or Latino</th>
<th>South Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>K304E</td>
<td>1.25%</td>
<td>0.44%</td>
<td>0.09%</td>
<td>&lt;0.02%</td>
<td>0.63%</td>
<td>&lt;0.05%</td>
</tr>
<tr>
<td>R181C</td>
<td>0.01%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>&lt;0.02%</td>
<td>0.02%</td>
<td>0.00%</td>
</tr>
<tr>
<td>S220L</td>
<td>0.01%</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
</tr>
</tbody>
</table>
This test is expected to detect 64% of carriers of European descent for this condition.

Pre-test and post-test carrier risks for the 23andMe PGS Carrier Status Test for MCAD Deficiency

<table>
<thead>
<tr>
<th></th>
<th>Carrier detection rate for this test</th>
<th>Pre-test (average) carrier risk</th>
<th>Post-test carrier risk for result “0 Variants Detected”</th>
</tr>
</thead>
<tbody>
<tr>
<td>European</td>
<td>64%</td>
<td>1 in 100</td>
<td>1 in 280</td>
</tr>
<tr>
<td>Other ethnicities*</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

*This condition is not as well studied in other ethnicities.

**Accuracy**

23andMe performed a method comparison study to assess the accuracy of the assay. Results of the test were compared with sequencing results for 150 samples with known variant status. Agreement between the two methods was >99% for all samples analyzed. The 95% confidence interval was 97.0% to 100%.

**Precision/Reproducibility**

A study was performed to assess the precision of the test. A total of 3,240 sample replicates were run across different testing conditions. This study yielded correct results for >99% of samples across all conditions tested. The study had >99% reproducibility and >99% repeatability.

**References**

Gregersen N et al. (1993). "Medium-chain acyl-CoA dehydrogenase (MCAD) deficiency: the prevalent mutation G985 (K304E) is subject to a strong founder effect from northwestern Europe." Hum Hered. 43(6):342-50.


Neuronal Ceroid Lipofuscinosis (CLN5-Related)

*Indications for Use*

The 23andMe PGS Carrier Status Test for Neuronal Ceroid Lipofuscinosis (CLN5-related NCL) is indicated for the detection of the Y392X variant in the CLN5 gene. This test is intended to be used to determine carrier status for CLN5-related NCL in adults, but cannot determine if a person has two copies of a tested variant. The test is most relevant for people of Finnish descent.

*Special considerations*

- There are currently no professional guidelines in the U.S. for carrier testing for this condition.

*Clinical performance*

The variant covered by this test is most common in people of Finnish descent. About 1 in 108 people (0.93%) of Finnish descent is a carrier for CLN5-related NCL.

Frequency of CLN5 variants in 23andMe customers

<table>
<thead>
<tr>
<th>Variant name</th>
<th>European</th>
<th>African American</th>
<th>Ashkenazi Jewish</th>
<th>East Asian</th>
<th>Hispanic or Latino</th>
<th>South Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>Y392X</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
</tr>
</tbody>
</table>

This test is expected to detect 94% of carriers of Finnish descent for this condition.

Pre-test and post-test carrier risks for the 23andMe PGS Carrier Status Test for CLN5-related NCL

<table>
<thead>
<tr>
<th></th>
<th>Carrier detection rate for this test</th>
<th>Pre-test (average) carrier risk</th>
<th>Post-test carrier risk for result “0 Variants Detected”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finnish</td>
<td>94%</td>
<td>1 in 108</td>
<td>1 in 1,800</td>
</tr>
<tr>
<td>Other ethnicities*</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

*This condition is not as well studied in other ethnicities.

*Accuracy*

23andMe performed a method comparison study to assess the accuracy of the assay. Results of the test were compared with sequencing results for 48 samples with known variant status. Agreement between the two methods was >99% for all samples analyzed. The 95% confidence interval was 91.5% to 100%.
Precision/Reproducibility

A study was performed to assess the precision of the test. A total of 1,080 sample replicates were run across different testing conditions. This study yielded correct results for >99% of samples across all conditions tested. The study had >99% reproducibility and >99% repeatability.

Selected References

Mole SE et al. (1993). "Neuronal Ceroid-Lipofuscinoses"


Additional references included in the report.

Neuronal Ceroid Lipofuscinosis (PPT1-Related)

Indications for Use

The 23andMe PGS Carrier Status Test for Neuronal Ceroid Lipofuscinosis (PPT1-related NCL) is indicated for the detection of 3 variants in the PPT1 gene. This test is intended to be used to determine carrier status for PPT1-related NCL in adults, but cannot determine if a person has two copies of a tested variant. The test is most relevant for people of Finnish descent.

Special considerations

• There are currently no professional guidelines in the U.S. for carrier testing for this condition.

Clinical performance

The variants covered by this test are most common in people of Finnish descent. About 1 in 64 people (1.52%) of Finnish descent is a carrier for PPT1-related NCL.

Frequency of PPT1 variants in 23andMe customers

<table>
<thead>
<tr>
<th>Variant name</th>
<th>European</th>
<th>African American</th>
<th>Ashkenazi Jewish</th>
<th>East Asian</th>
<th>Hispanic or Latino</th>
<th>South Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>R151X</td>
<td>0.09%</td>
<td>0.04%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.05%</td>
<td>0.00%</td>
</tr>
<tr>
<td>T75P</td>
<td>0.02%</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.01%</td>
<td>0.00%</td>
</tr>
<tr>
<td>R122W</td>
<td>0.02%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
</tr>
</tbody>
</table>
This test is expected to detect 98% of carriers of Finnish descent for this condition.

Pre-test and post-test carrier risks for the 23andMe PGS Carrier Status Test for PPT1-related NCL

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Carrier detection rate for this test</th>
<th>Pre-test (average) carrier risk</th>
<th>Post-test carrier risk for result “0 Variants Detected”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finnish</td>
<td>98%</td>
<td>1 in 64</td>
<td>1 in 3,200</td>
</tr>
<tr>
<td>Northern European</td>
<td>59%</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>Western European</td>
<td>59%</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>Other ethnicities*</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

*This condition is not as well studied in other ethnicities.

**Accuracy**

23andMe performed a method comparison study to assess the accuracy of the assay. Results of the test were compared with sequencing results for 148 samples with known variant status. Agreement between the two methods was >99% for all samples analyzed. The 95% confidence interval was 97.0% to 100%.

**Precision/Reproducibility**

A study was performed to assess the precision of the test. A total of 3,510 sample replicates were run across different testing conditions. This study yielded correct results for >99% of samples across all conditions tested. The study had >99% reproducibility and >99% repeatability.

**References**


Mole SE et al. (1993). "Neuronal Ceroid-Lipofuscinoses"


**Niemann-Pick Disease Type A**

**Indications For Use**

The 23andMe PGS Carrier Status Test for Niemann-Pick Disease Type A is indicated for the detection of 3 variants in the SMPD1 gene. This test is intended to be used to
determine carrier status for Niemann-Pick disease type A in adults, but cannot determine if a person has two copies of a tested variant. The test is most relevant for people of Ashkenazi Jewish descent.

Special considerations

- Carrier testing for Niemann-Pick disease type A is recommended by ACMG for people of Ashkenazi Jewish descent considering having children. This test includes the 3 variants recommended for testing by ACMG.

Clinical performance

The variants covered by this test are most common in people of Ashkenazi Jewish descent. About 1 in 90 people (1.11%) of Ashkenazi Jewish descent is a carrier for Niemann-Pick disease type A.

Frequency of SMPD1 variants in 23andMe customers

<table>
<thead>
<tr>
<th>Variant name</th>
<th>European</th>
<th>African American</th>
<th>Ashkenazi Jewish</th>
<th>East Asian</th>
<th>Hispanic or Latino</th>
<th>South Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>L302P</td>
<td>0.01%</td>
<td>0.00%</td>
<td>0.12%</td>
<td>0.00%</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
</tr>
<tr>
<td>fsP330</td>
<td>0.01%</td>
<td>0.00%</td>
<td>0.35%</td>
<td>0.00%</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
</tr>
<tr>
<td>R496L</td>
<td>0.01%</td>
<td>&lt;0.01%</td>
<td>0.47%</td>
<td>0.00%</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
</tr>
</tbody>
</table>

This test is expected to detect 97% of carriers of Ashkenazi Jewish descent for this condition.

Pre-test and post-test carrier risks for the 23andMe PGS Carrier Status Test for Niemann-Pick Disease Type A

<table>
<thead>
<tr>
<th></th>
<th>Carrier detection rate for this test</th>
<th>Pre-test (average) carrier risk</th>
<th>Post-test carrier risk for result “0 Variants Detected”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ashkenazi Jewish</td>
<td>97%</td>
<td>1 in 90</td>
<td>1 in 3,000</td>
</tr>
<tr>
<td>Other ethnicities*</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

*This condition is not as well studied in other ethnicities.

Accuracy

23andMe performed a method comparison study to assess the accuracy of the assay. Results of the test were compared with sequencing results for 146 samples with known variant status. Agreement between the two methods was >99% for all samples analyzed. The 95% confidence interval was 97.0% to 100%.
**Precision/Reproducibility**

A study was performed to assess the precision of the test. A total of 3,240 sample replicates were run across different testing conditions. This study yielded correct results for >99% of samples across all conditions tested. The study had >99% reproducibility and >99% repeatability.

**Selected References**


Additional references included in the report.

**Nijmegen Breakage Syndrome**

**Indications or Use**

The 23andMe PGS Carrier Status Test for Nijmegen Breakage Syndrome is indicated for the detection of the 657del5 variant in the NBN gene. This test is intended to be used to determine carrier status for Nijmegen breakage syndrome in adults, but cannot determine if a person has two copies of a tested variant. The test is most relevant for people of Eastern European (particularly Czech) descent.

**Special considerations**

- There are currently no professional guidelines in the U.S. for carrier testing for this condition.

**Clinical performance**

The variant covered by this test is most common in people of Eastern European descent. About 1 in 154 people (0.65%) of Eastern European (particularly Czech) descent is a carrier for Nijmegen breakage syndrome.

**Frequency of NBN variants in 23andMe customers**

<table>
<thead>
<tr>
<th>Variant name</th>
<th>European</th>
<th>African American</th>
<th>Ashkenazi Jewish</th>
<th>East Asian</th>
<th>Hispanic or Latino</th>
<th>South Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>657del5</td>
<td>0.09%</td>
<td>0.01%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.04%</td>
<td>0.00%</td>
</tr>
</tbody>
</table>

This test is expected to detect more than 99% of carriers of Eastern European descent for this condition.
Pre-test and post-test carrier risks for the 23andMe PGS Carrier Status Test for Nijmegen Breakage Syndrome

<table>
<thead>
<tr>
<th>Carrier detection rate for this test</th>
<th>Pre-test (average) carrier risk</th>
<th>Post-test carrier risk for result “0 Variants Detected”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eastern European (particularly Czech)</td>
<td>&gt; 99%</td>
<td>1 in 154</td>
</tr>
<tr>
<td>Other ethnicities*</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

*This condition is not as well studied in other ethnicities.

**Accuracy**

23andMe performed a method comparison study to assess the accuracy of the assay. Results of the test were compared with sequencing results for 47 samples with known variant status. Agreement between the two methods was >99% for all samples analyzed. The 95% confidence interval was 91.0% to 100%.

**Precision/Reproducibility**

A study was performed to assess the precision of the test. A total of 1,080 sample replicates were run across different testing conditions. This study yielded correct results for >99% of samples across all conditions tested. The study had >99% reproducibility and >99% repeatability.

**References**


Chrzanowska KH et al. (2012). "Nijmegen breakage syndrome (NBS)." Orphanet J Rare Dis. 7:13.
Indications for Use

The 23andMe PGS Carrier Status Test for Nonsyndromic Hearing Loss and Deafness, DFNB1 (GJB2-Related) is indicated for the detection of 2 variants in the GJB2 gene. This test is intended to be used to determine carrier status for DFNB1 in adults, but cannot determine if a person has two copies of a tested variant. The test is most relevant for people of European and Ashkenazi Jewish descent.

Special considerations

- The severity of hearing loss can vary, but there are no other symptoms associated with this condition.
- There are currently no professional guidelines in the U.S. for carrier testing for this condition.

Clinical performance

The variants covered by this test are most common in people of European and Ashkenazi Jewish descent. About 1 in 30 people (3.33%) of European descent and 1 in 16 people (6.25%) of Ashkenazi Jewish descent are carriers for DFNB1. This test does not include the majority of GJB2 variants that cause DFNB1 in people of East Asian descent.

Frequency of GJB2 variants in 23andMe customers

<table>
<thead>
<tr>
<th>Variant name</th>
<th>European</th>
<th>African American</th>
<th>Ashkenazi Jewish</th>
<th>East Asian</th>
<th>Hispanic or Latino</th>
<th>South Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>35delG</td>
<td>1.87%</td>
<td>0.55%</td>
<td>0.72%</td>
<td>&lt;0.02%</td>
<td>1.50%</td>
<td>&lt;0.05%</td>
</tr>
<tr>
<td>167delT</td>
<td>0.09%</td>
<td>0.02%</td>
<td>3.19%</td>
<td>0.00%</td>
<td>0.07%</td>
<td>0.00%</td>
</tr>
</tbody>
</table>

This test is expected to detect 76% of carriers of Ashkenazi Jewish descent and 79% of carriers of European descent for this condition.

Pre-test and post-test carrier risks for the 23andMe PGS Carrier Status Test for DFNB1

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Carrier detection rate for this test</th>
<th>Pre-test (average) carrier risk</th>
<th>Post-test carrier risk for result “0 Variants Detected”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ashkenazi Jewish</td>
<td>76%</td>
<td>1 in 16</td>
<td>1 in 63</td>
</tr>
<tr>
<td>European</td>
<td>79%</td>
<td>1 in 33</td>
<td>1 in 150</td>
</tr>
<tr>
<td>East Asian</td>
<td>&lt;1%</td>
<td>1 in 30</td>
<td>1 in 30</td>
</tr>
<tr>
<td>Other ethnicities*</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

*This condition is not as well studied in other ethnicities.
Accuracy

23andMe performed a method comparison study to assess the accuracy of the assay. Results of the test were compared with sequencing results for 103 samples with known variant status. Agreement between the two methods was >99% for all samples analyzed. The 95% confidence interval was 95.8% to 100%.

Precision/Reproducibility

A study was performed to assess the precision of the test. A total of 1,080 sample replicates were run across different testing conditions. This study yielded correct results for >99% of samples across all conditions tested. The study had >99% reproducibility and >99% repeatability.

References


Pendred Syndrome and DFNB4 Hearing Loss

Indications for Use

The 23andMe PGS Carrier Status Test for Pendred Syndrome and DFNB4 Hearing Loss is indicated for the detection of 6 variants in the SLC26A4 gene. This test is intended to be used to determine carrier status for Pendred syndrome and DFNB4 in adults, but cannot determine if a person has two copies of a tested variant. The test is most relevant for people of European and Japanese descent.

Special considerations

- Symptoms of Pendred syndrome and DFNB4 vary in severity depending on which variants are causing the condition.
- This test does not include a large fraction of SLC26A4 variants that cause Pendred syndrome or DFNB4 in any ethnicity.
- There are currently no professional guidelines in the U.S. for carrier testing for this condition.

Clinical performance

The variants covered by this test are most common in people of European and Japanese descent.

Frequency of SLC26A4 variants in 23andMe customers

<table>
<thead>
<tr>
<th>Variant name</th>
<th>European</th>
<th>African American</th>
<th>Ashkenazi Jewish</th>
<th>East Asian</th>
<th>Hispanic or Latino</th>
<th>South Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>L236P</td>
<td>0.10%</td>
<td>0.01%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.03%</td>
<td>0.00%</td>
</tr>
<tr>
<td>E384G</td>
<td>0.06%</td>
<td>0.02%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.02%</td>
<td>0.00%</td>
</tr>
<tr>
<td>T416P</td>
<td>0.06%</td>
<td>0.02%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.03%</td>
<td>0.00%</td>
</tr>
<tr>
<td>V138F</td>
<td>0.05%</td>
<td>0.03%</td>
<td>0.02%</td>
<td>0.00%</td>
<td>0.02%</td>
<td>0.00%</td>
</tr>
<tr>
<td>H723R</td>
<td>&lt;0.01%</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
<td>0.30%</td>
<td>0.01%</td>
<td>0.00%</td>
</tr>
<tr>
<td>L445W</td>
<td>0.03%</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
<td>&lt;0.02%</td>
<td>0.03%</td>
<td>0.00%</td>
</tr>
</tbody>
</table>

This test is expected to detect 40-60% of carriers of European descent and 35-45% of carriers of Japanese descent for this condition.

Pre-test and post-test carrier risks for the 23andMe PGS Carrier Status Test for Pendred Syndrome and DFNB4

<table>
<thead>
<tr>
<th></th>
<th>Carrier detection rate for this test</th>
<th>Pre-test (average) carrier risk</th>
<th>Post-test carrier risk for result “0 Variants Detected”</th>
</tr>
</thead>
<tbody>
<tr>
<td>European</td>
<td>40-60%</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>Japanese</td>
<td>35-45%</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>
Other ethnicities* | Unknown | Unknown | Unknown
---|---|---|---
*This condition is not as well studied in other ethnicities.

**Accuracy**

23andMe performed a method comparison study to assess the accuracy of the assay. Results of the test were compared with sequencing results for 292 samples with known variant status. Agreement between the two methods was >99% for all samples analyzed. The 95% confidence interval was 98.5% to 100%.

**Precision/Reproducibility**

A study was performed to assess the precision of the test. A total of 6,480 sample replicates were run across different testing conditions. This study yielded correct results for >99% of samples across all conditions tested. The study had >99% reproducibility and >99% repeatability.

**Selected References**


Additional references included in the report.

**Primary Hyperoxaluria Type 2**

**Indications for Use**

The 23andMe PGS Carrier Status Test for Primary Hyperoxaluria Type 2 (PH2) is indicated for the detection of the 103delG variant in the GRHPR gene. This test is intended to be used to determine carrier status for PH2 in adults, but cannot determine if a person has two copies of a tested variant.

**Special considerations**

- This test does not include a large fraction of GRHPR variants that cause PH2.
- There are currently no professional guidelines in the U.S. for carrier testing for this condition.
Clinical performance

The variant covered by this test is most common in people of European descent.

Frequency of GRHPR variants in 23andMe customers

<table>
<thead>
<tr>
<th>Variant name</th>
<th>European</th>
<th>African American</th>
<th>Ashkenazi Jewish</th>
<th>East Asian</th>
<th>Hispanic or Latino</th>
<th>South Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>103delG</td>
<td>0.10%</td>
<td>0.04%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.03%</td>
<td>0.00%</td>
</tr>
</tbody>
</table>

This test is expected to detect 68% of carriers of European descent for this condition.

Pre-test and post-test carrier risks for the 23andMe PGS Carrier Status Test for PH2

<table>
<thead>
<tr>
<th></th>
<th>Carrier detection rate for this test</th>
<th>Pre-test (average) carrier risk</th>
<th>Post-test carrier risk for result “0 Variants Detected”</th>
</tr>
</thead>
<tbody>
<tr>
<td>European</td>
<td>68%</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>Other ethnicities*</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

*This condition is not as well studied in other ethnicities.

Accuracy

23andMe performed a method comparison study to assess the accuracy of the assay. Results of the test were compared with sequencing results for 49 samples with known variant status. Agreement between the two methods was >99% for all samples analyzed. The 95% confidence interval was 91.5% to 100%.

Precision/Reproducibility

A study was performed to assess the precision of the test. A total of 1,080 sample replicates were run across different testing conditions. This study yielded correct results for >99% of samples across all conditions tested. The study had >99% reproducibility and >99% repeatability.

Selected References


Additional references included in the report.
Rhizomelic Chondrodysplasia Punctata Type 1 (RCDP1)

Indications for Use

The 23andMe PGS Carrier Status Test for Rhizomelic Chondrodysplasia Punctata Type 1 (RCDP1) is indicated for the detection of the L292X variant in the PEX7 gene. This test is intended to be used to determine carrier status for RCDP1 in adults, but cannot determine if a person has two copies of a tested variant.

Special considerations

- This test does not include a large fraction of PEX7 variants that cause RCDP1 in any ethnicity.
- There are currently no professional guidelines in the U.S. for carrier testing for this condition.

Clinical performance

The variant covered by this test is most common in people of European descent.

Frequency of PEX7 variants in 23andMe customers

<table>
<thead>
<tr>
<th>Variant name</th>
<th>European</th>
<th>African American</th>
<th>Ashkenazi Jewish</th>
<th>East Asian</th>
<th>Hispanic or Latino</th>
<th>South Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>L292X</td>
<td>0.15%</td>
<td>0.05%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.07%</td>
<td>&lt;0.05%</td>
</tr>
</tbody>
</table>

This test is expected to detect about 50% of carriers of European descent for this condition.

Pre-test and post-test carrier risks for the 23andMe PGS Carrier Status Test for RCDP1

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Carrier detection rate for this test</th>
<th>Pre-test (average) carrier risk</th>
<th>Post-test carrier risk for result “0 Variants Detected”</th>
</tr>
</thead>
<tbody>
<tr>
<td>European</td>
<td>About 50%</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>Other ethnicities*</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

*This condition is not as well studied in other ethnicities.

Accuracy

23andMe performed a method comparison study to assess the accuracy of the assay. Results of the test were compared with sequencing results for 49 samples with known variant status. Agreement between the two methods was >99% for all samples analyzed. The 95% confidence interval was 91.5% to 100%.
Precision/Reproducibility

A study was performed to assess the precision of the test. A total of 1,080 sample replicates were run across different testing conditions. This study yielded correct results for >99% of samples across all conditions tested. The study had >99% reproducibility and >99% repeatability.

Selected References

Braverman NE et al. (1993). "Rhizomelic Chondrodysplasia Punctata Type 1"


Additional references included in the report.

Sickle Cell Anemia

Indications for Use

The 23andMe PGS Carrier Status Test for Sickle Cell Anemia is indicated for the detection of the HbS variant in the HBB gene. This test is intended to be used to determine carrier status for sickle cell anemia in adults, but cannot determine if a person has two copies of the tested variant. The test is most relevant for people of African descent.

Special considerations

• Carrier screening for hemoglobinopathies such as sickle cell anemia is recommended by ACOG for people of African descent.

Clinical performance

The variant covered by this test is most common in people of African descent. About 1 in 12 people (8.33%) of African American descent is a carrier for sickle cell anemia.

Frequency of the HbS variant in 23andMe customers

<table>
<thead>
<tr>
<th>Variant name</th>
<th>European</th>
<th>African American</th>
<th>Ashkenazi Jewish</th>
<th>East Asian</th>
<th>Hispanic or Latino</th>
<th>South Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbS</td>
<td>0.03%</td>
<td>6.73%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.71%</td>
<td>0.15%</td>
</tr>
</tbody>
</table>

This test is expected to detect more than 99% of carriers for this condition.
Pre-test and post-test carrier risks for the 23andMe PGS Carrier Status Test for Sickle Cell Anemia

<table>
<thead>
<tr>
<th></th>
<th>Carrier detection rate for this test</th>
<th>Pre-test (average) carrier risk</th>
<th>Post-test carrier risk for result “0 Variants Detected”</th>
</tr>
</thead>
<tbody>
<tr>
<td>African American*</td>
<td>&gt;99%</td>
<td>1 in 12</td>
<td>-</td>
</tr>
<tr>
<td>African</td>
<td>&gt;99%</td>
<td>Varies by country</td>
<td>-</td>
</tr>
</tbody>
</table>

*This test covers the only variant that causes sickle cell anemia.

**Accuracy**

23andMe performed a method comparison study to assess the accuracy of the assay. Results of the test were compared with sequencing results for 54 samples with known variant status. Agreement between the two methods was >99% for all samples analyzed. The 95% confidence interval was 92.1% to 100%.

**Precision/Reproducibility**

A study was performed to assess the precision of the test. A total of 1,350 sample replicates were run across different testing conditions. This study yielded correct results for >99% of samples across all conditions tested. The study had >99% reproducibility and >99% repeatability.

**Selected References**

Bender MA et al. (1993). "Sickle Cell Disease"

Additional references included in the report.

**Sjögren-Larsson Syndrome**

**Indications for Use**

The 23andMe PGS Carrier Status Test for Sjögren-Larsson Syndrome is indicated for the detection of the P315S variant in the ALDH3A2 gene. This test is intended to be used to determine carrier status for Sjögren-Larsson syndrome in adults, but cannot determine if a person has two copies of a tested variant. The test is most relevant for people of Swedish descent.

**Special considerations**

- There are currently no professional guidelines in the U.S. for carrier testing for this condition.
**Clinical performance**

The variant covered by this test is most common in people of Swedish descent. About 1 in 200 people (0.50%) of Swedish descent is a carrier for Sjögren-Larsson syndrome.

**Frequency of ALDH3A2 variants in 23andMe customers**

<table>
<thead>
<tr>
<th>Variant name</th>
<th>European</th>
<th>African</th>
<th>Ashkenazi Jewish</th>
<th>East Asian</th>
<th>Hispanic or Latino</th>
<th>South Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>P315S</td>
<td>0.01%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
</tr>
</tbody>
</table>

This test is expected to detect 84% of carriers of Swedish descent for this condition.

**Pre-test and post-test carrier risks for the 23andMe PGS Carrier Status Test for Sjögren-Larsson Syndrome**

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Carrier detection rate for this test</th>
<th>Pre-test (average) carrier risk</th>
<th>Post-test carrier risk for result “0 Variants Detected”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Swedish</td>
<td>84%</td>
<td>1 in 200</td>
<td>1 in 1,200</td>
</tr>
<tr>
<td>Other ethnicities*</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

*This condition is not as well studied in other ethnicities.

**Accuracy**

23andMe performed a method comparison study to assess the accuracy of the assay. Results of the test were compared with sequencing results for 79 samples with known variant status. Agreement between the two methods was >99% for all samples analyzed. The 95% confidence interval was 94.5% to 100%.

**Precision/Reproducibility**

A study was performed to assess the precision of the test. A total of 1,080 sample replicates were run across different testing conditions. This study yielded correct results for >99% of samples across all conditions tested. The study had >99% reproducibility and >99% repeatability.

**Selected References**


Additional references included in the report.
Tay-Sachs Disease

Indications for Use

The 23andMe PGS Carrier Status Test for Tay-Sachs Disease is indicated for the detection of 4 variants in the HEXA gene. This test is intended to be used to determine carrier status for Tay-Sachs disease in adults, but cannot determine if a person has two copies of a tested variant. The test is most relevant for people of Ashkenazi Jewish and Cajun descent.

Special considerations

- Symptoms of this disease vary in severity depending on which variants are causing the condition.
- Carrier testing for Tay-Sachs disease is recommended by ACMG for people of Ashkenazi Jewish descent considering having children. This test includes the 3 variants recommended for testing by ACMG.
- This test does not cover variants causing Tay-Sachs disease that are more common in people of French Canadian descent.

Clinical performance

The variants covered by this test are most common in people of Ashkenazi Jewish and Cajun descent. About 1 in 31 people (3.23%) of Ashkenazi Jewish descent, 1 in 30 people (3.33%) of Cajun descent, and 1 in 30 people (3.33%) of French Canadian descent are carriers for Tay-Sachs disease.

Frequency of HEXA variants in 23andMe customers

<table>
<thead>
<tr>
<th>Variant name</th>
<th>European</th>
<th>African American</th>
<th>Ashkenazi Jewish</th>
<th>East Asian</th>
<th>Hispanic or Latino</th>
<th>South Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>G269S</td>
<td>0.07%</td>
<td>&lt;0.01%</td>
<td>0.21%</td>
<td>0.00%</td>
<td>0.03%</td>
<td>0.00%</td>
</tr>
<tr>
<td>1278insTATC</td>
<td>0.13%</td>
<td>0.02%</td>
<td>2.85%</td>
<td>&lt;0.02%</td>
<td>0.05%</td>
<td>&lt;0.05%</td>
</tr>
<tr>
<td>IVS12+1G&gt;C</td>
<td>0.02%</td>
<td>&lt;0.01%</td>
<td>0.65%</td>
<td>0.00%</td>
<td>0.01%</td>
<td>0.00%</td>
</tr>
<tr>
<td>IVS9+1G&gt;A</td>
<td>0.10%</td>
<td>0.02%</td>
<td>0.00%</td>
<td>&lt;0.02%</td>
<td>0.04%</td>
<td>0.00%</td>
</tr>
</tbody>
</table>

This test is expected to detect 99% of carriers of Ashkenazi Jewish descent and more than 99% of carriers of Cajun descent for this condition.
Pre-test and post-test carrier risks for the 23andMe PGS Carrier Status Test for Tay-Sachs Disease

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Carrier detection rate for this test</th>
<th>Pre-test (average) carrier risk</th>
<th>Post-test carrier risk for result “0 Variants Detected”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ashkenazi Jewish</td>
<td>99%</td>
<td>1 in 31</td>
<td>1 in 2,700</td>
</tr>
<tr>
<td>Cajun</td>
<td>&gt;99%</td>
<td>1 in 30</td>
<td>1 in 29,000,000</td>
</tr>
<tr>
<td>French Canadian</td>
<td>&lt;10%</td>
<td>1 in 30</td>
<td>Unknown</td>
</tr>
<tr>
<td>Other ethnicities*</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

*This condition is not as well studied in other ethnicities.

**Accuracy**

23andMe performed a method comparison study to assess the accuracy of the assay. Results of the test were compared with sequencing results for 199 samples with known variant status. Agreement between the two methods was >99% for all samples analyzed. The 95% confidence interval was 94.9% to 100%.

**Precision/Reproducibility**

A study was performed to assess the precision of the test. A total of 10,260 sample replicates were run across different testing conditions. This study yielded correct results for >99% of samples across all conditions tested. The study had >99% reproducibility and >99% repeatability.

**References**


**Tyrosinemia Type I**

**Indications for Use**

The 23andMe PGS Carrier Status Test for Tyrosinemia Type I is indicated for the detection of 4 variants in the FAH gene. This test is intended to be used to determine
carrier status for tyrosinemia type I in adults, but cannot determine if a person has two copies of a tested variant. The test is most relevant for people of French Canadian and Finnish descent.

Special considerations

- There are currently no professional guidelines in the U.S. for carrier testing for this condition.

Clinical performance

The variants covered by this test are most common in people of French Canadian, Ashkenazi Jewish, and Finnish descent. About 1 in 21 people (4.76%) of French Canadian descent, 1 in 150 people (0.67%) of Ashkenazi Jewish descent, and 1 in 123 people (0.81%) of Finnish descent are carriers for tyrosinemia type I.

Frequency of FAH variants in 23andMe customers

<table>
<thead>
<tr>
<th>Variant name</th>
<th>European</th>
<th>African</th>
<th>Ashkenazi</th>
<th>East</th>
<th>Hispanic</th>
<th>South</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>American</td>
<td>Jewish</td>
<td>Asian</td>
<td>or Latino</td>
<td>Asian</td>
</tr>
<tr>
<td>W262X</td>
<td>&lt;0.01%</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
</tr>
<tr>
<td>P261L</td>
<td>0.02%</td>
<td>&lt;0.01%</td>
<td>0.74%</td>
<td>&lt;0.02%</td>
<td>0.01%</td>
<td>0.00%</td>
</tr>
<tr>
<td>IVS12+5G&gt;A</td>
<td>0.09%</td>
<td>0.04%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.02%</td>
<td>0.05%</td>
</tr>
<tr>
<td>IVS6-1G&gt;T</td>
<td>0.04%</td>
<td>&lt;0.01%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.04%</td>
<td>0.00%</td>
</tr>
</tbody>
</table>

This test is expected to detect 90% of carriers of French Canadian descent, more than 99% of carriers of Ashkenazi Jewish descent, and 86% of carriers of Finnish descent for this condition.

Pre-test and post-test carrier risks for the 23andMe PGS Carrier Status Test for Tyrosinemia Type I

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Carrier detection rate for this test</th>
<th>Pre-test (average) carrier risk</th>
<th>Post-test carrier risk for result “0 Variants Detected”</th>
</tr>
</thead>
<tbody>
<tr>
<td>French Canadian</td>
<td>90%</td>
<td>1 in 21</td>
<td>1 in 200</td>
</tr>
<tr>
<td>Ashkenazi Jewish</td>
<td>&gt;99%</td>
<td>1 in 150</td>
<td>1 in 149,000,000</td>
</tr>
<tr>
<td>Finnish</td>
<td>86%</td>
<td>1 in 123</td>
<td>1 in 870</td>
</tr>
<tr>
<td>European</td>
<td>60%</td>
<td>1 in 150</td>
<td>1 in 370</td>
</tr>
<tr>
<td>Turkish</td>
<td>30%</td>
<td>1 in 150</td>
<td>1 in 210</td>
</tr>
<tr>
<td>Other ethnicities*</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

*This condition is not as well studied in other ethnicities.
Accuracy

23andMe performed a method comparison study to assess the accuracy of the assay. Results of the test were compared with sequencing results for 196 samples with known variant status. Agreement between the two methods was >99% for all samples analyzed. The 95% confidence interval was 97.7% to 100%.

Precision/Reproducibility

A study was performed to assess the precision of the test. A total of 4,320 sample replicates were run across different testing conditions. This study yielded correct results for >99% of samples across all conditions tested. The study had >99% reproducibility and >99% repeatability.

References


Sniderman King L et al. (1993). "Tyrosinemia Type I"


Usher Syndrome Type 1F

Indications for Use

The 23andMe PGS Carrier Status Test for Usher Syndrome Type 1F (Usher 1F) is indicated for the detection of the R245X variant in the PCDH15 gene. This test is intended to be used to determine carrier status for Usher 1F in adults, but cannot determine if a person has two copies of a tested variant. The test is most relevant for people of Ashkenazi Jewish descent.
Special considerations

• There are currently no professional guidelines in the U.S. for carrier testing for this condition.

Clinical performance

The variant covered by this test is most common in people of Ashkenazi Jewish descent. About 1 in 147 people (0.68%) of Ashkenazi Jewish descent is a carrier for Usher 1F.

Frequency of PCDH15 variants in 23andMe customers

<table>
<thead>
<tr>
<th>Variant name</th>
<th>European</th>
<th>African American</th>
<th>Ashkenazi Jewish</th>
<th>East Asian</th>
<th>Hispanic or Latino</th>
<th>South Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>R245X</td>
<td>0.02%</td>
<td>&lt;0.01%</td>
<td>0.87%</td>
<td>0.00%</td>
<td>0.03%</td>
<td>0.00%</td>
</tr>
</tbody>
</table>

This test is expected to detect 91% of carriers of Ashkenazi Jewish descent for this condition.

Pre-test and post-test carrier risks for the 23andMe PGS Carrier Status Test for Usher 1F

<table>
<thead>
<tr>
<th></th>
<th>Carrier detection rate for this test</th>
<th>Pre-test (average) carrier risk</th>
<th>Post-test carrier risk for result “0 Variants Detected”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ashkenazi Jewish</td>
<td>91%</td>
<td>1 in 147</td>
<td>1 in 1,600</td>
</tr>
<tr>
<td>Other ethnicities*</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

*This condition is not as well studied in other ethnicities.

Accuracy

23andMe performed a method comparison study to assess the accuracy of the assay. Results of the test were compared with sequencing results for 47 samples with known variant status. Agreement between the two methods was >99% for all samples analyzed. The 95% confidence interval was 91.3% to 100%.

Precision/Reproducibility

A study was performed to assess the precision of the test. A total of 1,080 sample replicates were run across different testing conditions. This study yielded correct results for >99% of samples across all conditions tested. The study had >99% reproducibility and >99% repeatability.

References


Usher Syndrome Type 3A

**Indications for Use**

The 23andMe PGS Carrier Status Test for Usher Syndrome Type 3A (Usher 3A) is indicated for the detection of the N48K variant in the CLRN1 gene. This test is intended to be used to determine carrier status for Usher 3A in adults, but cannot determine if a person has two copies of a tested variant. The test is most relevant for people of Ashkenazi Jewish descent.

**Special considerations**

- The test does not include the majority of CLRN1 variants that cause Usher 3A in people of Finnish descent.
- There are currently no professional guidelines in the U.S. for carrier testing for this condition.

**Clinical performance**

The variant covered by this test is most common in people of Ashkenazi Jewish descent. About 1 in 120 people (0.83%) of Ashkenazi Jewish descent is a carrier for Usher 3A.

**Frequency of CLRN1 variants in 23andMe customers**

<table>
<thead>
<tr>
<th>Variant name</th>
<th>European</th>
<th>African American</th>
<th>Ashkenazi Jewish</th>
<th>East Asian</th>
<th>Hispanic or Latino</th>
<th>South Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>N48K</td>
<td>0.02%</td>
<td>&lt;0.01%</td>
<td>1.06%</td>
<td>0.00%</td>
<td>0.01%</td>
<td>0.00%</td>
</tr>
</tbody>
</table>

This test is expected to detect 93% of carriers of Ashkenazi Jewish descent for this condition.

**Pre-test and post-test carrier risks for the 23andMe PGS Carrier Status Test for Usher 3A**

<table>
<thead>
<tr>
<th></th>
<th>Carrier detection rate for this test</th>
<th>Pre-test (average) carrier risk</th>
<th>Post-test carrier risk for result “0 Variants Detected”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ashkenazi Jewish</td>
<td>93%</td>
<td>1 in 120</td>
<td>1 in 1,700</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>Finnish</td>
<td>Other ethnicities*</td>
<td></td>
</tr>
<tr>
<td>----------------</td>
<td>---------</td>
<td>-------------------</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;10%</td>
<td>Unknown</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Unknown</td>
<td>Unknown</td>
<td></td>
</tr>
</tbody>
</table>

*This condition is not as well studied in other ethnicities.

**Accuracy**

23andMe performed a method comparison study to assess the accuracy of the assay. Results of the test were compared with sequencing results for 49 samples with known variant status. Agreement between the two methods was >99% for all samples analyzed. The 95% confidence interval was 91.5% to 100%.

**Precision/Reproducibility**

A study was performed to assess the precision of the test. A total of 1,080 sample replicates were run across different testing conditions. This study yielded correct results for >99% of samples across all conditions tested. The study had >99% reproducibility and >99% repeatability.

**References**


**Zellweger Syndrome Spectrum (PEX1-Related)**

**Indications for Use**

The 23andMe PGS Carrier Status Test for Zellweger Syndrome Spectrum (PEX1-related ZSS) is indicated for the detection of the G843D variant in the PEX1 gene. This test is intended to be used to determine carrier status for PEX1-related ZSS in adults, but cannot determine if a person has two copies of a tested variant.
Special considerations

- This test does not include the majority of PEX1 variants that cause ZSS in any ethnicity.
- There are currently no professional guidelines in the U.S. for carrier testing for this condition.

Clinical performance

The variant covered by this test is rare in all ethnicities.

Frequency of PEX1 variants in 23andMe customers

<table>
<thead>
<tr>
<th>Variant name</th>
<th>European</th>
<th>African American</th>
<th>Ashkenazi Jewish</th>
<th>East Asian</th>
<th>Hispanic or Latino</th>
<th>South Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>G843D</td>
<td>0.13%</td>
<td>0.06%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.05%</td>
<td>0.00%</td>
</tr>
</tbody>
</table>

This test is expected to detect 35% of carriers for this condition.

Pre-test and post-test carrier risks for the 23andMe PGS Carrier Status Test for PEX1-related ZSS

<table>
<thead>
<tr>
<th></th>
<th>Carrier detection rate for this test</th>
<th>Pre-test (average) carrier risk</th>
<th>Post-test carrier risk for result “0 Variants Detected”</th>
</tr>
</thead>
<tbody>
<tr>
<td>European</td>
<td>41%</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>All ethnicities*</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

* This condition is not as well studied in other ethnicities.

Accuracy

23andMe performed a method comparison study to assess the accuracy of the assay. Results of the test were compared with sequencing results for 49 samples with known variant status. Agreement between the two methods was >99% for all samples analyzed. The 95% confidence interval was 91.5% to 100%.

Precision/Reproducibility

A study was performed to assess the precision of the test. A total of 1,080 sample replicates were run across different testing conditions. This study yielded correct results for >99% of samples across all conditions tested. The study had >99% reproducibility and >99% repeatability.
Selected References


Steinberg SJ et al. (1993). "Peroxisome Biogenesis Disorders, Zellweger Syndrome Spectrum"

Additional references included in the report.

References
Data on file at 23andMe, Mountain View, CA

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Mountain View, CA 94041-1225

Contact us:
Customer Care: 1-800-239-5230
customercare.23andme.com

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PI Revision Date October 2015

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